Published in final edited form as:

Endocr Pract. 2019 June ; 25(6): 517–525. doi:10.4158/EP-2018-0527.

IMPAIRED AWARENESS OF HYPOGLYCEMIA CONTINUES TO BE A RISK FACTOR FOR SEVERE HYPOGLYCEMIA DESPITE THE USE OF CONTINUOUS GLUCOSE MONITORING SYSTEM IN TYPE 1 DIABETES

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Abstract

Objective: Impaired awareness of hypoglycemia (IAH) is a risk factor for severe hypoglycemia in patients with type 1 diabetes (T1D) not using a continuous glucose monitoring (CGM) system. The current study investigated the prevalence of IAH and its relationship with severe hypoglycemia in T1D patients using CGM systems.

Methods: This cross-sectional observational study enrolled 135 patients with T1D and ongoing real-time CGM use. A survey was conducted to assess hypoglycemia awareness with the Gold, Clarke, and Pedersen-Bjergaard questionnaires and the 6-month history of severe hypoglycemia. Other diabetes histories and the CGM glucose data were collected.

Results: The Gold, Clarke, and Pedersen-Bjergaard questionnaires demonstrated the overall prevalence of IAH/abnormal awareness to be 33.3%, 43.7%, and 77.0%, respectively. Participant age and duration of T1D were consistently related to IAH or hypoglycemia unawareness with all three questionnaires ($P < .05$). Amongst the patients using CGM for >6 months, 24.5% were found to have at least one episode of severe hypoglycemia in the preceding 6 months. IAH identified by the Gold and Clarke questionnaires and hypoglycemia unawareness identified by the Pedersen-Bjergaard questionnaire were related to 6-, 4.63-, and 5.83-fold increased risk of severe hypoglycemia ($P = .001$, $.004$, and $.013$), respectively. IAH identified by the Gold/Clarke questionnaires was associated with a longer duration of CGM glucose <54 mg/dL and higher glucose coefficients of variation ($P < .05$).

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

Conclusion: IAH is highly prevalent and related to a higher risk for severe hypoglycemia in T1D patients using CGM.

INTRODUCTION

Hypoglycemia is a major barrier for glucose control in patients with type 1 diabetes (T1D) (1). Recurrent hypoglycemia can lead to the development of impaired awareness of hypoglycemia (IAH), a condition in which patients experience an attenuation of hypoglycemic symptoms, leading to the inability to recognize the occurrence of a hypoglycemic event (1,2). Without the recognition and immediate treatment for a hypoglycemic episode, the blood glucose can continue to decrease and result in severe hypoglycemia and other complications, including seizures, coma, emergency room visits, and potentially death (3–6). For patients with IAH and recurrent severe hypoglycemia, pancreas or islet transplantation can be considered as potential treatment options (7,8). Indeed, islet transplantation has been proven to restore hypoglycemia awareness and significantly improve counterregulatory hormone responses (9). While these therapies may eventually become the cure for T1D, transplant medicine is currently limited by graft availability, cost, and the need for dedicated life-long immunosuppressant use.

Real-time continuous glucose monitoring (CGM) systems are devices which provide immediately available information about blood glucose levels and glycemic trends as frequently as every 5 minutes. These devices can also alert patients to hypoglycemic events (10). With the hypoglycemia alerts, a patient wearing a CGM device can administer treatment to prevent the development or progression of hypoglycemia (11,12). Indeed, recent studies demonstrated that real-time CGM use lowers the incidence of severe hypoglycemic events (13–15).

While the prevalence and risk factors for IAH and severe hypoglycemia have been examined in T1D patients, most studies reported the hypoglycemia awareness status for the non-CGM using population (16–22). Little information exists about the prevalence of, and risk factors for, IAH and severe hypoglycemia in T1D patients utilizing CGM. Furthermore, as patients wearing CGM devices, including those with IAH, will receive alerts for their hypoglycemic episodes, it could be questioned whether IAH remains a significant risk factor for severe hypoglycemia and continues to be a public health threat for this population. The current study aimed to address these knowledge gaps by evaluating the prevalence and risk factors for IAH and severe hypoglycemia, and assessing the relationship between IAH and severe hypoglycemia in the T1D patients using CGM.

METHODS

Study Design

A cross-sectional observational study was conducted from May through September 2018. The University of Utah Institution Review Board approved the current study. All patients provided informed consent before participating in the study.

Study Cohort and Recruitment

Patients with T1D and using CGM at the University of Utah Endocrinology Clinic System (one university campus and four community clinics) were approached for study recruitment. The inclusion criteria were age ≥ 18 years with a history of T1D and current real-time CGM use. Use of an insulin pump linked to a CGM with programmed automated insulin adjustment/suspension was an exclusion criterion. A medical chart review was conducted for all participants to confirm eligibility.

Study Procedure and Measures

All participants completed a study survey that documented the duration of T1D and CGM use, severe hypoglycemic events in the preceding 6 months, and hypoglycemia awareness status. A severe hypoglycemic event was defined as a hypoglycemic episode requiring assistance for treatment administration (23). Hypoglycemia awareness status was determined by the Gold (16), Clarke (17), and Pedersen-Bjergaard (18) questionnaires. In short, the Gold questionnaire asks individuals to report their experience in detecting hypoglycemic events with scores ranging from 1 (always aware) to 7 (never aware) in a Likert-type scale. The Clarke questionnaire is comprised of eight questions assessing patients' experience during hypoglycemic events. A score (0 to 7) is calculated based on the responses to these questions. For both the Gold and Clarke questionnaires, a score ≥ 4 suggests IAH; a score ≤ 2 suggests normal hypoglycemia awareness; and a score of 3 represents undetermined awareness status. The Pedersen-Bjergaard questionnaire asks individuals to report whether they recognize symptoms during hypoglycemic events and, based on the answer, the hypoglycemia awareness status is categorized as "normal," "impaired awareness," or "unawareness." All of these questionnaires have been previously validated based on their associations with severe hypoglycemia. Specifically, the Gold questionnaire was validated with prospective recording of severe hypoglycemic episodes in patients with matched characteristics (16). The Clarke questionnaire was assessed through both retrospective recalls and prospective records of severe hypoglycemia (17) as well as hypoglycemic clamps (24). The Pedersen-Bjergaard questionnaire was first validated with retrospective recalls of severe hypoglycemic events (25), followed by a revision with both retrospective and prospective reports (18).

For each participant, a medical chart review was conducted to collect demographic and medical information, including age, sex, insulin regimen (multiple daily injections, insulin pump, or others), and the most recent hemoglobin A1C (HbA1c). For the participants whose CGM data were available, their CGM data in the preceding 2 weeks were collected, including the duration of time in hypoglycemia (CGM glucose <54 and ≥ 70 mg/dL), glucose coefficients of variation (as measurements of glycemic variability), and percentage of time with glucose records, which was used as an indicator for the duration of active CGM usage.

Statistical Analysis

Only data from those participants meeting the eligibility criteria were used for the statistical analysis. For analyses assessing the prevalence and risk factors for severe hypoglycemia in the preceding 6 months, participants using CGM for less than 6 months were excluded in order to eliminate severe hypoglycemic events prior to the CGM use.

Demographic characteristics were summarized using the mean/standard deviation or median/range, and proportion as appropriate. Chi-squared analyses were used as appropriate to evaluate the relationships between participant sex, insulin regimen, hypoglycemia awareness, and 6-month severe hypoglycemia history. Logistic regression analyses were used to evaluate the relationships between age, the age of T1D onset, duration of T1D/CGM use, recent HbA1c with hypoglycemia awareness status and severe hypoglycemia history, and the relationships between the Gold and Clarke scoring and severe hypoglycemia history. Logistic regression analysis was also used to evaluate the relationships between the total duration of hypoglycemia and glucose coefficients of variation on CGMs with hypoglycemia awareness status and severe hypoglycemia history. For the Pedersen-Bjergaard questionnaire, separate analyses were conducted between normal awareness and abnormal awareness (i.e., impaired awareness plus unawareness) groups and between normal awareness and unawareness groups for the above analyses. Linear regression analysis was conducted to determine the correlation between the Gold and Clarke scores. A *P*-value of <.05 was considered to be statistically significant.

RESULTS

Study Population

A total of 135 patients with T1D and ongoing CGM use were recruited for the study (Table 1). Versions G4, G5, and G6 of the Dexcom CGM were used in 9/135 (7%), 97/135 (78%), and 17/135 (14%) patients, respectively. One patient used a Medtronic CGM with the Guardian 3 sensor (0.7%). Amongst the 124/135 (92%) patients with available CGM data, the mean and standard deviation percentage of CGM usage time was $84.5 \pm 18.7\%$. Specifically, 103 (83%) and 91 (73%) of these 124 patients had 70% and 80% of active CGM usage time, respectively.

Prevalence of IAH and Risk Factors

Impaired or abnormal hypoglycemia awareness was identified in 45/135 (33.3%), 59/135 (43.7%), and 104/135 (77.0%) patients by the Gold, Clarke, and Pedersen-Bjergaard questionnaires, respectively. Of the 77.0% of patients with abnormal hypoglycemia awareness identified by the Pedersen-Bjergaard questionnaire, 79 (58.5%) patients were identified to have impaired awareness, and 25 (18.5%) patients were determined to have hypoglycemia unawareness (Fig. 1).

Amongst the factors assessed for their relationships with the impaired awareness status (Table 2), longer duration of T1D and patient age were consistently related both to impaired awareness identified with the Gold and Clarke questionnaires and to unawareness identified with the Pedersen-Bjergaard questionnaire. Longer duration of CGM use was related to impaired awareness identified with the Gold questionnaire. Participant age at T1D onset, recent HbA1c levels, sex, and insulin regimen (Supplemental Table S1) were not related to impaired awareness/unawareness status.

Prevalence of Severe Hypoglycemia and Risk Factors

Amongst the 135 recruited patients, 102 patients used CGM for more than 6 months. Twenty-five of these 102 patients (24.5%) reported having at least one event of severe hypoglycemia, with a median of two severe hypoglycemic episodes (range, 1 to 12), in the preceding 6 months. Furthermore, IAH was identified in 35 and 46 of these 102 patients based on the Gold and Clarke questionnaires, with the prevalence of positive severe hypoglycemia history being 15/35 (42.9%) and 18/46 (39.1%), respectively. For the Pedersen-Bjergaard questionnaire, impaired awareness and complete unawareness were identified in 78 and 22 of the 102 patients, with the prevalence of positive severe hypoglycemia history being 22/78 (28.2%) and 10/22 (45.5%), respectively. There was no relationship between the 6-month severe hypoglycemia history and participants' age, sex, the age of T1D onset, duration of T1D/CGM use, HbA1c, or insulin regimen (Supplemental Table S2).

Assessment of the Relationship Between Severe Hypoglycemia and IAH

IAH identified by the Gold and Clarke questionnaires was related to increased odds of severe hypoglycemia in the preceding 6 months by 6.00-fold (95% confidence interval [CI], 1.826 to 16.5; $P = .001$) and 4.63-fold (95% CI, 1.55 to 12.3; $P = .004$), respectively. While impaired awareness identified by the Pedersen-Bjergaard questionnaire tended to be related to higher odds of severe hypoglycemia (odds ratio 2.75; $P = .12$), hypoglycemia unawareness was related to 5.83-fold increased odds of severe hypoglycemia (95% CI, 1.39 to 21.9; $P = .013$). Scores on both the Gold and Clarke questionnaires were also related to severe hypoglycemia (Fig. 2). Specifically, each increment in the Gold and Clarke scoring increased the odds of severe hypoglycemia by 1.58- and 1.71-fold ($P < .001$), respectively.

Assessment of the Relationships Between the Duration of Hypoglycemia and Glucose Glycemic Variability With IAH and Severe Hypoglycemia

For the 92% of patients with available CGM data, IAH identified by the Gold and Clarke questionnaires was associated with a longer duration of hypoglycemia with CGM glucose < 54 mg/dL (95% CI, 1.03 to 1.79; $P = .028$ and 95% CI, 1.02 to 1.85; $P = .037$, respectively) (Fig. 3) and also tended to be associated with a longer duration of glucose < 70 mg/dL (95% CI, 1.00 to 1.20; $P = .053$ and 95% CI, 0.99 to 1.19; $P = .097$, respectively). IAH identified by the Gold and Clarke questionnaires was also associated with higher glucose coefficients of variation ($P = .039$ and $P = .025$, respectively) (Fig. 4). Abnormal awareness/unawareness identified by the Pedersen-Bjergaard questionnaire were not associated with a longer duration of hypoglycemia or higher glucose coefficients of variation.

Amongst the patients using CGMs for more than 6 months, severe hypoglycemia tended to be associated with higher glucose coefficients of variation ($P = .051$) but not a longer duration of hypoglycemia.

Assessing the Relationship Between Hypoglycemia Questionnaires

Abnormalities identified on any of the Gold, Clarke, and Pedersen-Bjergaard questionnaires were highly associated with abnormalities identified on other questionnaires ($P < .001$)

(Supplemental Table S3). The Gold and Clarke scores were also significantly correlated ($R = 0.668$; $P < .001$).

DISCUSSION

The current study demonstrated that IAH and severe hypoglycemia were highly prevalent in T1D patients with ongoing real-time CGM use. Also, IAH identified by the Gold and Clarke questionnaires and hypoglycemia unawareness identified by the Pedersen-Bjergaard questionnaire were risk factors for severe hypoglycemia in the current study population. Incremental increases in Gold/Clarke scoring were correlated with higher risks of severe hypoglycemia. IAH identified by the Gold and Clarke questionnaires, but not the Pedersen-Bjergaard questionnaire, was also associated with a longer duration of hypoglycemia with CGM glucose < 54 mg/dL and higher glycemic variabilities. Age and the duration of T1D appeared to be potential risk factors for IAH/hypoglycemia unawareness. The positivity of IAH/hypoglycemia unawareness identified by test questionnaires was highly related, and the Gold/Clarke scores were also significantly correlated.

Prior studies examining the prevalence of IAH and evaluating IAH as a risk factor for severe hypoglycemia were conducted either before the widespread clinical availability of CGM (16–20) or in the T1D population not using CGM (21,22). These studies demonstrated that the prevalence of IAH ranged from about 25% (Gold and Clarke questionnaires) to 60% (Pedersen-Bjergaard questionnaire, with 40 to 50% in the impaired awareness category and 10 to 15% in the unawareness category) (19,20,26). In these studies, IAH was associated with a 3- to 20-fold increased risk for severe hypoglycemia (19,20). On the other hand, the recent studies reporting hypoglycemia awareness in the CGM population were mainly clinical trials testing the effect of CGM on improving hypoglycemia awareness and course (13,27,28). With the nature of the interventional design, many factors of these studies may have altered the participants' hypoglycemia awareness, including study eligibility criteria, patient education, and follow-up visits for study protocols (29). Thus, the data from these clinical trials might not represent the general patient population. Little information exists describing the “real-world” status of hypoglycemia awareness and its relationship with severe hypoglycemia for the population using CGM.

In the current study, IAH/hypoglycemia unawareness was associated with about a 6-fold increased risk for severe hypoglycemia. In addition, amongst the characteristics examined, IAH/hypoglycemia unawareness was the only risk factor for severe hypoglycemia identified for the T1D population using CGM. These findings suggest that IAH, despite the use of CGM, is still an important clinical problem for T1D patients. Furthermore, one would expect CGM and its alerting system to mitigate and possibly eliminate the additional risk for severe hypoglycemia associated with IAH by alerting the patients about hypoglycemic episodes. However, the patients with IAH continued to have a significantly higher risk for experiencing severe hypoglycemia compared to those without IAH in the current cohort. These observations suggest that the mechanism by which IAH contributes to the development of severe hypoglycemia is different from the other traditional risk factors. Prior studies have shown that IAH is closely associated with hypoglycemia-associated autonomic failure (HAAF) (30). HAAF represents the loss of counterregulatory hormonal responses

during hypoglycemia and is considered an independent factor contributing to the development of severe hypoglycemia (31). As CGM intervention does not improve the autonomic function in T1D patients with HAAF (28), the underlying HAAF may have contributed to the development of severe hypoglycemia in the IAH cohort.

In the current analysis, the prevalence of IAH in CGM users appeared to be higher than that previously reported in the non-CGM using population (16–20). Moreover, amongst the risk factors assessed, longer duration of CGM use was related to a higher risk for IAH identified by the Gold questionnaire, and concomitant insulin pump use was not found to be related to hypoglycemia awareness as demonstrated in a previous study (27). One possible explanation for these possibly counterintuitive observations is the presence of an indication bias, as patients with IAH were preferentially initiated on CGM and insulin pumps by their care providers. Furthermore, the IAH risk factors evaluated, either positive or negative, were mostly consistent across all tested questionnaires. In contrast, previous studies in non-CGM using populations demonstrated a discordance in the risk factors for IAH (16–20). It remains unclear whether this difference was related to the patient selection for CGM implementation or that the CGM intervention made impacts on the risk factors related to the presentation of IAH.

About one-fourth of our study cohort had a history of severe hypoglycemia in the preceding 6 months. This prevalence was even higher in the patients with IAH/hypoglycemia unawareness and similar to a recent clinical trial assessing CGM intervention in an IAH population (32% of patients developing severe hypoglycemia over a 6-month period; IAH identified by the Clarke questionnaire) (13). Overall, aligning with the findings from prior CGM clinical trials (13,27,32), the current analyses suggested that severe hypoglycemia continues to be a clinical challenge despite the use of CGM. Moreover, several traditional risk factors for severe hypoglycemia in non-CGM users were not identified to be related to severe hypoglycemia in our study cohort. In particular, while an earlier clinical trial determined that HbA1c correlated closely with severe hypoglycemic episodes (33), the current analyses suggested that a lower HbA1c was not associated with a higher risk for severe hypoglycemia in the population using CGM. This observation is consistent with prior CGM interventional studies demonstrating that CGM supported the lowering of HbA1c without increasing hypoglycemic events (14,34), while the use of new insulin analogs or insulin pumps may also play a significant role as suggested by the T1D Exchange Clinic Registry (35).

IAH identified by the Gold and Clarke questionnaires was associated with a longer duration with CGM glucose <54 mg/dL, but this association was not as clear for the duration with glucose <70 mg/dL. One may argue that patients with IAH might not be able to treat themselves in a timely manner or have underlying HAAF. Thus, with the loss of these counterregulatory mechanisms, these patients were prone to develop a worse hypoglycemia course. As hypoglycemia has been shown to increase glycemic variabilities (36), this relationship between IAH and worse hypoglycemia course may also help explain the association between IAH and higher glycemic variabilities. Similarly, abnormal awareness/unawareness identified by the Pedersen-Bjergaard questionnaire was not associated with a longer duration of hypoglycemia and thus not related to higher glycemic variabilities.

However, it remains unclear why there was a lack of association between the abnormal awareness/unawareness identified by the Pedersen-Bjergaard questionnaire with a longer duration of hypoglycemia, in contrast to IAH identified by the Gold/Clarke questionnaires.

IAH/hypoglycemia unawareness, as determined by all three of the tested hypoglycemia awareness questionnaires, was significantly related to a risk for severe hypoglycemia. Also, IAH identified by the Gold and Clarke questionnaires was associated with a longer duration of hypoglycemia with glucose <54 mg/dL and higher glycemic variabilities. Overall, the current study supports the use of the Gold and Clarke questionnaires to identify the IAH in T1D patients using CGM. Furthermore, the Gold and Clarke scores demonstrated an incremental change in the severe hypoglycemia risk for each increase in scoring. Therefore, the current analyses may support the use these scoring systems for future research requiring measurements of small changes in hypoglycemia awareness, such as identifying interventions to improve hypoglycemia awareness in CGM users.

In the current study, patient-reported history of severe hypoglycemia was used to evaluate the prevalence and risk factors for severe hypoglycemia. This study method was shown to be valid in prior hypoglycemia awareness and CGM studies (17,18,20,22,27,37).

The current study has several strengths but also some limitations. To our knowledge, this is the first study to report the prevalence of IAH in nonclinical trial settings and to demonstrate the relationship between IAH and severe hypoglycemia in CGM users. The commonly used hypoglycemia awareness questionnaires were utilized. Also, medical chart reviews were conducted to confirm the study variables such as T1D diagnosis, insulin regimen, and ongoing CGM use and to eliminate the data from CGM with automated insulin pump programs. However, the current study was observational and thus cannot provide mechanistic explanations for the relationships identified, including whether IAH directly contributes to the development of severe hypoglycemia. As a cross-sectional study, the current study was also not designed to prospectively determine whether CGM and concomitant insulin pump usage alter hypoglycemia awareness and mitigate the risk for severe hypoglycemia. Also, the participants on CGM may have better insurance coverage, which may potentially reflect their socioeconomic status and thus bias the study cohort.

We did not exclude participants for their CGM insertion sites to reflect the “real-world” status, while some non-Food and Drug Administration approved insertion sites may still provide accurate glucose values (38). Moreover, the current study did not include—and thus cannot represent—data for the flash intermittent glucose monitoring system, a glucose monitoring technology without a hypoglycemia alert system.

CONCLUSION

IAH is highly prevalent and continues to be a significant risk factor for severe hypoglycemia in T1D patients despite the use of CGM. Further therapeutic options are needed to improve hypoglycemia awareness and further mitigate the risk for severe hypoglycemia in this patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENT

This study was supported by the DRC at Washington University, Grant No. 2 P30 DK020579, and the University of Utah Diabetes and Metabolism Center. We appreciate all the assistance from the faculties, nurses, and medical assistants for the current study. We also thank all the study participants, without whom this study would not have been possible.

Abbreviations:

CGM	continuous glucose monitoring
CI	confidence interval
HAAF	hypoglycemia-associated autonomic failure
HbA1c	hemoglobin A1C
IAH	impaired awareness of hypoglycemia
T1D	type 1 diabetes

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Fig. 1.

Bar graph showing the prevalence of hypoglycemia awareness status identified by the Gold, Clarke, and Pedersen-Bjergaard questionnaires in type 1 diabetes patients using continuous glucose monitoring. The prevalence of impaired awareness identified by the Gold and Clarke questionnaires was 33% and 44%, respectively. The prevalence of impaired awareness and unawareness identified by the Pedersen-Bjergaard questionnaire was 58.5% and 18.5%, respectively.

Fig. 2. Logistic regression plots for severe hypoglycemia history in the preceding 6 months and the (A) Gold and (B) Clarke scores. *OR* = odds ratio.

Fig. 3.

Logistic regression plots for hypoglycemia awareness status identified by the (A) Gold and (B) Clarke questionnaires and the duration of time with continuous glucose monitoring (CGM) glucose less than 54 mg/dL. *IAH*= impaired awareness of hypoglycemia; *OR* = odds ratio.

Fig. 4.

Logistic regression plots for hypoglycemia awareness status identified by the (A) Gold and (B) Clarke questionnaires and the continuous glucose monitoring (CGM) glucose coefficients of variation. *IAH*= impaired awareness of hypoglycemia; *OR* = odds ratio.

Table 1

Study Population Demographics

Age, mean years $\pm$ SD	41.8 $\pm$ 15.5
Sex, female/male, n (%)	81/54 (60/40)
Age of T1D onset, mean years $\pm$ SD	21.5 $\pm$ 14.1
Duration of T1D, mean years $\pm$ SD	20.3 $\pm$ 14.3
Duration of CGM use, median years (range)	2 (0.13–10)
HbA1c, mean% $\pm$ SD	7.6 $\pm$ 1.3 ^a
Insulin pump/MDI use, n (%)	88/47 (65/35)

Abbreviations: CGM = continuous glucose monitoring; HbA1c = hemoglobin A1C; MDI = multiple daily injections; T1D = type 1 diabetes.

^aHbA1c 7.6% is equivalent to 59.6 mmol/mol.

Table 2

Assessments of Risk Factors for Impaired Awareness of Hypoglycemia in T1D CGM Users

	OR	95% CI	P value
<i>Age (years)</i>			
Gold	1.04	1.02–1.07	.002
Clarke	1.05	1.02–1.07	.002
PB (nl vs. abnl)	1.02	0.99–1.05	.129
PB (nl vs. unaware)	1.04	1.00–1.08	.045
<i>Age of T1D onset (years)</i>			
Gold	0.98	0.96–1.01	.229
Clarke	0.98	0.95–1.01	.148
PB (nl vs. abnl)	1.00	0.97–1.03	.810
PB (nl vs. unaware)	0.98	0.94–1.03	.472
<i>Duration of T1D (years)</i>			
Gold	1.08	1.04–1.11	<.001
Clarke	1.08	1.04–1.11	<.001
PB (nl vs. abnl)	1.03	1.00–1.06	.062
PB (nl vs. unaware)	1.06	1.01–1.10	.009
<i>Duration of CGM use (years)</i>			
Gold	1.21	1.02–1.45	.029
Clarke	1.13	0.95–1.33	.166
PB (nl vs. abnl)	1.09	0.90–1.33	.392
PB (nl vs. unaware)	1.25	0.97–1.81	.084
<i>HbA1c (%)</i>			
Gold	0.84	0.61–1.14	.262
Clarke	0.78	0.59–1.05	.099
PB (nl vs. abnl)	0.85	0.64–1.13	.269
PB (nl vs. unaware)	0.82	0.54–1.24	.343

Abbreviations: abnl = abnormal awareness; CI = confidence interval; CGM = continuous glucose monitoring; HbA1c = hemoglobin A1C; nl = normal awareness; OR = odds ratio; PB = Pedersen-Bjergaard; T1D = type 1 diabetes.