Time of Day When Type 1 Diabetes Patients With Eating Disorder Symptoms Most Commonly Restrict Insulin

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ABSTRACT

Objective: Restricting insulin to lose weight is a significant problem in the clinical management of type 1 diabetes (T1D). Little is known about this behavior or how to effectively intervene. Identifying when insulin restriction occurs could allow clinicians to target typical high-risk times or formulate hypotheses regarding factors that influence this behavior. The current study investigated the frequency of insulin restriction by time of day.

Methods: Fifty-nine adults with T1D and eating disorder symptoms completed 72 hours of real-time reporting of eating and insulin dosing with continuous glucose monitoring. We used a generalized estimating equation model to test the global hypothesis that frequency of insulin restriction (defined as not taking enough insulin to cover food consumed) varied by time of day, and examined frequency of insulin restriction by hour. We also examined whether patterns of insulin restriction for 72 hours corresponded with patients' interview reports of insulin restriction for the past 28 days.

Results: Frequency of insulin restriction varied as a function of time ($p = .016$). Insulin restriction was the least likely in the morning hours (6:00–8:59 AM), averaging 6% of the meals/snacks consumed. Insulin restriction was more common in the late afternoon (3:00–5:59 PM), peaking at 29%. Insulin was restricted for 32% of the meals/snacks eaten overnight (excluding for hypoglycemia); however, overnight eating was rare. Insulin restriction was associated with higher 120-minute postprandial blood glucose (difference = 44.4 mg/dL, 95% confidence interval = 22.7–68.5, $p < .001$) and overall poorer metabolic control ($r = 0.43$–0.62, p's $< .01$). Patients reported restricting insulin for a greater percentage of meals and snacks for the past 28 days than during the 72 hour real-time assessment; however, the reports were correlated (Spearman's $\rho = 0.46$, $p < .001$) and accounted for similar variance in HbA_{1c} (34% versus 35%, respectively).

Conclusions: Findings suggest that insulin restriction may be less likely in the morning, and that late afternoon is a potentially important time for additional therapeutic support. Results also suggest that systematic clinical assessment and treatment of overnight eating might improve T1D management.

Key words: adherence, compliance, eating disorder(s), insulin administration, type 1 diabetes.

INTRODUCTION

A significant subset of individuals with type 1 diabetes (T1D) evidence eating disorder symptoms, including the intentional withholding of insulin to lose weight (reported by 30%–40% of young women with T1D) (1,2). Restricting insulin, while exceedingly dangerous, is highly effective for weight control (3–5). Without insulin, glucose cannot enter fat or muscle cells from the bloodstream. If the blood glucose exceeds 180 mg/dL (in most people), the excess glucose is excreted into the urine. Thus, individuals with diabetes are able to overeat or even binge without gaining weight, as sugar (or calories) is "purged" via urination. Without glucose as a cellular energy source, the body also breaks down fat for energy, which results in weight loss. However, chronic hyperglycemia facilitates the development of the microvascular complications of diabetes, such as retinopathy, neuropathy, and nephropathy (3,4,6). The breakdown of fat for energy also results in the release of acids (or ketones) into the bloodstream, which at high levels are toxic. Restricting insulin triples the risk for early and severe diabetes-related medical complications (including diabetic ketoacidosis) and is the single best predictor of premature death among patients with T1D (3).

Although several studies document the prevalence and impact of intentional insulin restriction (e.g., 2,3,7), little is known about the factors associated with this behavior or when it is most likely to occur. A better understanding of typical patterns of insulin

CGM = continuous glucose monitoring, **EDE** = Eating Disorder Examination, **EMA** = ecological momentary assessment, **HbA_{1c}** = glycated hemoglobin, **T1D** = type 1 diabetes

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restriction could advance intervention for this high-risk patient population. For example, identifying when insulin restriction is most common could enable clinicians to use mobile technologies to deliver additional therapeutic support to patients at times when it is most needed. Such therapeutic support could be provided without having to rely on patients' self-awareness, which may be poor, particularly in times of stress. Identifying times when restricting insulin is most common might also generate hypotheses regarding contextual variables associated with this dangerous weight control practice. For example, if patients restrict insulin most commonly for the first meal of the day, this might suggest different contributing factors than if patients restrict most commonly for the last meal of the day.

The aim of the current study was to investigate whether restriction of short-acting insulin among T1D patients with eating disorder symptoms varied by time of day. We examined patterns of insulin restriction by hour based on 72 hours of real-time reporting of eating and insulin dosing in the natural environment. We also examined whether patterns of insulin restriction for 72 hours corresponded with patients' interview reports of insulin restriction for the past 28 days. The clinical relevance of insulin restriction was examined by calculating correlations between insulin restriction and glucose metabolic control. Specifically, we examined the relationship between insulin restriction and postprandial blood glucose, as well as the relationship between frequency of insulin restriction (as a raw frequency and as a percentage of meals/snacks consumed) and mean blood glucose.

RESEARCH DESIGN AND METHODS

Participants

Participants were recruited as part of a larger study that used ecological momentary assessment (EMA) to identify real-time precursors to eating disorder behavior in the participant's natural environment (see Merwin et al., 2015 (8)). The parent study included 72 hours of real-time reporting of mood and behavior and continuous glucose monitoring (CGM), assessment of HbA_{1c}, a diagnostic interview, and self-report measures (not included in the current report) collected between December 2011 and June 2014. The total sample consisted of 82 adults (older than 18 years) with T1D: 63 adults with T1D who screened positive for clinically significant eating disorder symptoms and 18 healthy T1D control participants. Only the clinical sample was used for the current report.

Participants were considered a positive screen for eating disorder symptoms if they scored 20 or higher on the Diabetes Eating Problems Survey-Revised (DEPS-R) (9). The Diabetes Eating Problems Survey-Revised is a diabetes-specific self-report measure of eating disorder symptoms that includes items such as "*I feel fat when I take all of my insulin*," "*I try to keep my blood sugar high so that I will lose weight*," and "*I feel that my eating is out of control*." Scores at or higher than 20 have been associated with higher HbA_{1c} (9). Participants did not have to specifically endorse intentional insulin restriction for weight loss to be eligible, but rather could have indicated uncontrolled eating, distorted body image, or other eating disorder symptoms. Participants were ineligible if they indicated a history of psychosis or thought disorder or if they had cognitive deficits that interfered with independent management of their T1D or severe hypoglycemic unawareness that would present safety concerns (as determined by the Gold Method (10) and episodes in the last 2 years that required third party intervention).

Recruitment methods included online advertisements and e-mails sent to patient registries as well as flyers placed in endocrinology clinics at two major medical centers in the Southeast. Interested individuals were screened for eligibility by the clinical research coordinator. All procedures were approved by the Duke University Health Systems Institutional Review Board and informed consent was completed with qualified study staff.

Procedure

Participants completed 72 hours of momentary (or real-time) assessment of eating and insulin dosing in their natural environment. During this assessment, their blood glucose was monitored continuously using a blinded continuous glucose monitor. Participants provided a blood sample to assess HbA_{1c} and completed a clinician-administered semistructured diagnostic interview for eating disorders (Eating Disorder Examination (EDE) (11)), along with self-report measures not relevant to the current study.

Momentary Assessment

EMA gathers real-time data about an individual's behavior in their natural environment. Such data are thought to be less influenced by the artificial nature of the laboratory or the biases of retrospective recall (12). EMA typically makes use of mobile devices (e.g., electronic diaries) and can include random interval recording, event-based recording, or a combination of the two. During interval recording, participants receive a prompt to complete an assessment at random intervals within a specified timeframe (e.g., once an hour) throughout the day. In event-based recording, participants initiate an assessment when an "event" occurs (e.g., a meal). The current study used a combined interval and event-based recording scheme delivered via an automated telephone survey system (IfByPhone, Chicago, IL). Participants received random calls from IfByPhone to complete surveys once or twice an hour during waking hours (interval data not included in the current report) and also called in to the system to report eating episodes throughout the day.

Participants were instructed to call to report meals and snacks as close in time as possible to the eating episode. For each report, they completed a survey that required 2 to 3 minutes to complete (see the study by Merwin et al., 2015 (8) for additional methods). They reported when they had started eating and answered questions about the eating episode, including whether they administered adequate insulin ("*Did you take enough insulin to cover your food*?"). They responded to survey questions with telephone key presses. Participants were trained in the assessment procedures before beginning the 72-hour reporting period and were oriented to each of the survey questions. In the event insulin that was not required for a meal (e.g., a low-carbohydrate snack, hypoglycemia), participants were instructed to indicate they provided sufficient insulin for that meal. Participants were encouraged to be as honest as possible and to not change their typical behavior in any way.

During the 72-hour assessment, participants wore blinded continuous glucose monitoring systems (Medtronic iPro2, Minneapolis, MN). Glucose sensors were inserted by trained study staff. These sensors sampled interstitial glucose continuously, which the continuous glucose monitoring systems stored as 5-minute averages. Participants were provided with a OneTouch meter and test strips and were instructed to check their blood sugar 3 to 4 times a day to calibrate the CGM. CGM data were downloaded using specialized software that provided estimates of the percentage of time the individual was hypo- or hyperglycemic, among other parameters.

Eating Disorder Examination

The EDE is a widely used assessment for eating disorders and is considered the criterion standard in the eating disorder field (11,13). The EDE includes diagnostic items as well as items that quantify eating disorder symptom severity for the past 28 days. The EDE was used as a secondary measure of patterns of insulin restriction and used to examine whether the frequency of insulin restriction reported during the 72-hour EMA corresponded with participants' retrospective report of this behavior for the past 28 days. At the start of the clinician-administered interview, the patient was oriented to the appropriate period by recalling life events that had occurred during the past 4 weeks (e.g., an event with family or friends, a change in work schedule). Patients were then asked to recall their typical eating patterns during this

period. Specifically, they were asked: "*Over the past four weeks which of these meals or snacks have you eaten on a regular basis (breakfast, midmorning snack, lunch, midday snack, dinner, after dinner snack, nocturnal eating)?"* Responses vary from 0 to 28 days. In the typical scoring of the EDE, raw responses are used to assign a score on an ordinal scale (e.g., 0 = meal or snack not eaten; 1 = meal or snack eaten on 1 to 5 days; […] 6 = meal or snack eaten every day). However, for the current study, we used the actual counts of meals and snacks, rather than the ordinal score. We then asked a follow-up question about insulin restriction (not included in the original EDE): "*You said that you ate* [breakfast] [X times]. *How many times over the past four weeks did you provide yourself with sufficient/insufficient insulin to cover your eating for this meal?"* Omitting insulin because of hypoglycemia or giving less insulin unintentionally (e.g., miscalculation of insulin needs) was not counted as episodes of insulin restriction.

DATA ANALYTIC STRATEGY

Momentary (Real-Time) Assessment

To avoid pathologizing insulin omission that may have been required because of low or dropping blood sugar, we time-synced eating reports to participants' CGM data and excluded eating episodes that occurred when blood glucose was less than 70 mg/dL within 15 minutes of meal initiation. We calculated the frequency of insulin restriction by hour as a percentage of meals or snacks consumed for which insufficient insulin dosing was reported (i.e., patients indicated "no" to the prompt "Did you take enough insulin to cover your food?"). To maximize interpretability alongside the 28-day retrospective report, we also divided the day into six equal time bins (e.g., 6:00–8:59 AM, 9:00–11:59 AM) reflecting morning, midmorning, afternoon, midafternoon, evening, and late evening, with an additional "overnight" bin, which was longer (12:00–5:59 AM). We calculated the frequency of insulin restriction in each time bin as a percentage of meals or snacks consumed for which insufficient insulin dosing was reported. We used a generalized estimating equation (GEE) model to test the global hypothesis that the typical frequency of insulin restriction differed across time. The model was specified with a binary dependent variable (yes/no insulin restriction), time bin as a predictor, and a first-order autoregressive correlation structure to take into account possible within-person correlation. We then calculated contrasts that compared each time bin with all other time bins. The overnight bin was excluded because of sparseness.

Finally, we examined the impact of insulin restriction on metabolic control. We estimated a GEE model in which the dependent variable was 120-minute postprandial blood glucose, and the predictor variables were the insulin administration status (insulin restricted or not) and premeal blood glucose. The postprandial blood glucose level was transformed using the natural logarithm, and participant served as the clustering variable. When eating episodes were less than 120 minutes apart, we used only the second eating episode in the analysis to avoid using postprandial values that were affected by subsequent eating (and thus would be elevated, but not necessarily because of insulin restriction).

We also calculated partial correlation coefficients reflecting the relationship between the frequency of insulin restriction (both raw frequency and percentage of eating episodes) and glucose metabolic control, as indexed by mean CGM value and HbA_{1c}. HbA_{1c} value was determined by the assay Roche Tina-Quant. We controlled for insulin delivery method (i.e., insulin pump versus multiple daily injections) due to past research indicating that insulin pump use is associated with better metabolic control (14).

Given the lack of information on factors related to insulin restriction, we examined whether insulin restriction frequency was related to demographic variables. Partial correlational analyses were used to examine the relationship between insulin restriction frequency and age, body mass index (BMI), and time since diagnosis, controlling for number of meals. Analysis of covariance was used to examine whether there were differences in insulin restriction frequency as a function of age of onset of T1D (child versus adult onset) and insulin delivery method.

28-Day Retrospective Report

We calculated the frequency of insulin restriction for each individual as a percentage of reported meals and snacks consumed for which the participant reported insufficient insulin dosing. Percentages for each participant were calculated for total meals and snacks and for each of the seven categories of eating episodes (e.g., breakfast, midmorning snack, lunch). We calculated the correlation between the frequency of insulin restriction reported for 28 days and frequency reported for 72 hours. In addition, given observed differences in frequency counts between meals and snacks throughout the day, we conducted a proportions test to examine whether these differences were statistically significant. We also calculated partial correlation coefficients reflecting the relationship between the frequency of insulin restriction for 28 days and glucose metabolic control. A hierarchical linear regression was used to determine whether restricting insulin for snacks accounted for additional variance in HbA_{1c} above what was accounted for by the frequency of insulin restriction for meals and control variables (i.e., number of eating events and insulin delivery method).

RESULTS

Fifty-nine of the 63 participants had sufficient data to be included in the current report (five individuals did not complete the EMA and one participant did not complete the EDE and had insufficient data to calculate insulin restriction frequency during the 72-hour EMA). Table 1 summarizes sample demographics.

Compliance with the study protocol was high. Participants completed 96.3% (SD = 7.3%) of the random interval prompts (interval data reported elsewhere; see Merwin et al., 2015 (8)). On average, participants called in to report 12.78 (SD = 3.55) meals or snacks for 3 days. CGM calibration accuracy was good with a mean absolute difference % of 9.9.

Participants mean CGM value was 195.01 mg/dL (SD = 60.59 mg/dL). Participants' CGM values were greater than 180 mg/dL, on average, 48.3% (SD = 23.4%) of the time. HbA_{1c} ranged from 6.4% to 17.0% (M(SD)= 9.3% (2.5%)). Ninety-three percent of the participants had HbA_{1c} greater than 7%. Frequency of complications related to hyperglycemia is reported in Table 1.

Frequency of insulin restriction ranged from 0% to 100% of the meals/snacks that participants consumed for 72 hours, with a mean for the sample of 18.9% (SD = 25.2%). More than half of the participants (n = 33, 56.9%) reported insulin restriction at least once during the momentary assessment, 21 participants (36.2%) reported insulin restriction at least twice, 15 participants (25.9%) reported insulin restriction at least three times, and nine participants (15.5%) reported restricting insulin four or more times.

Insulin restriction was associated with metabolic glucose control. Blood glucose at 120 minutes postprandial was higher for the eating events when insulin was restricted (mean = 214.5 mg/dL, 95% CI = 195.2–235.6), compared with when insulin was not restricted (mean = 170.5 mg/dL, 95% CI = 162.7–178.6, $p < .001$; difference = 44.4 mg/dL, 95% CI = 22.7–68.5). Raw frequency of insulin restriction also correlated with participants' mean CGM value (r = 0.50, $p < .001$) and HbA_{1c} (r = 0.44, p = .001). The percentage of meals/snacks with insulin restriction also correlated with mean CGM value and HbA_{1c} as expected (Table 2).

Insulin restriction varied as a function of time, GEE global p value = .016 (n = 58, 525 total nonhypoglycemic eating episodes;

TABLE 1. Participant Demographics (N = 59)

Characteristic	M (SD) or *n* (%)
Age, y	41.3 (12.4)
Female sex	55 (93.2%)
Race/ethnicity	
White	50 (84.7%)
African-American/black	8 (13.6%)
Asian/Pacific-Islander	1 (1.7%)
Marital status	
Never married	14 (23.7%)
Married	36 (61.0%)
Separated/divorced	8 (13.6%)
Widowed	1 (1.7%)
Highest level of education	
High school graduate or GED	5 (8.5%)
Some college/technical school	14 (23.7%)
Bachelor's degree	30 (50.8%)
Graduate degree	10 (16.9%)
Age at type 1 diabetes diagnosis, y	19.0 (10.5)
Duration of type 1 diabetes, y	22.3 (13.4)
Treatment regimen	
Insulin pump therapy	37 (62.7%)
Multiple daily injections	22 (37.3%)
HbA_{1c}, %	9.25 (2.5)
HbA_{1c}, mmol/mol	78 (27.2)
History of retinopathy	17 (28.8%)
History of neuropathy	12 (20.3%)
History of nephropathy	9 (15.3%)
History of diabetes ketoacidosis	24 (40.7%)

y = years; GED = general equivalency diploma; HbA_{1c} = glycated hemoglobin.

103 with insulin restriction). Frequency of insulin restriction by time of day is summarized in Table 3. Observed proportion of eating episodes with insulin restriction is plotted in Figure 1 using hourly time bins.

Insulin restriction was the least common for meals/snacks consumed between 6:00 and 8:59 AM. Insulin was restricted, on average, for 6% of participants' total eating episodes during that period. Insulin restriction was more common for meals/snacks consumed in the late afternoon and peaked at 29% between 3:00 and 3:59 PM.

Meals/snacks consumed between 12:00 and 5:59 AM also had a high percentage of insulin restriction (particularly between 3:00 and 3:59 AM); however, this 6-hour time block also had the fewest number of eating episodes. Eighteen eating episodes were reported between 12:00 and 5:59 AM (3.4% of the total meals/snacks consumed during the 72 hours).

Results of the planned contrasts revealed morning (6:00–8:59 AM) restriction was significantly lower than the remaining time bins ($p < .001$) and late afternoon (3:00–5:59 PM) was significantly higher than all others ($p = .04$). The remaining contrasts were not statistically significant: midmorning (9:00–11:59 AM) versus all, $p = .90$; afternoon (12:00–2:59 PM) versus all, $p = .31$; evening (6:00–8:59 PM) versus all, $p = .67$; and late evening (9:00–11:59 PM) versus all, $p = .44$. The overnight bin was excluded.

Insulin restriction frequency was not related to any demographic variable (including age, BMI, age of onset of T1D, and time since diagnosis). It was related to current insulin delivery method, $F(1, 55) = 4.90$, $p = .004$. Individuals using multiple daily injections restricted insulin more frequently (M(SD) = 2.71 (3.39), $n = 21$) than those using an insulin pump (M(SD) = 1.24 (1.67), $n = 37$).

Participants reported restricting insulin for a greater percentage of meals/snacks for the past 28 days (M(SD) = 29.5% (25.5%)) than what was observed in the 72-hour real-time assessment, (M(SD) = 18.9% (25.2%)), although reports were correlated, Spearman's ρ correlation = 0.46, $p < .001$.

Table 4 summarizes data for the seven categories of eating episodes in the 28-day retrospective reports. Similar to the 72-hour real-time data, insulin restriction was higher in the midafternoon and for eating episodes that occurred overnight (although eating overnight was likewise rare). Overall, insulin restriction was more common for snacks (43.4%, 95% CI = 35.4–53.3) than for meals (23.2%, 95% CI = 17.4–31.0), $p < .001$ (analyses exclude nocturnal eating), but there were no significant differences by snack category (midmorning, midafternoon, or evening snack). The percentage of insulin restriction for meals was consistent throughout the day, with insulin restriction occurring approximately 23% of the time on average.

TABLE 2. Partial Correlations Between Insulin Restriction and Metabolic Control Controlling for Bolus Insulin Delivery Method

			Correlations					
	n	M (SD)	*1*	*2*	*3*	*4*	*5*	*6*
1 HbA_{1c}, %	56	9.25 (2.5)	1					
2 CGM mean	58	195.0 (60.6)	.78**	1				
3 28-day insulin restriction, freq	58	34.6 (33.7)	.65**	.47**	1			
4 28-day insulin restriction, %	58	29.5 (25.5)	.59**	.46*	.95**	1		
5 72-hour insulin restriction, freq	58	1.8 (2.5)	.44*	.50**	.55**	.56**	1	
6 72-hour insulin restriction, %	58	18.9 (25.2)	.58**	.52**	.62**	.65**	.91**	1

HbA_{1c} = glycated hemoglobin; CGM = continuous glucose monitoring; freq = frequency.

Partial correlations control for whether the individual reported using an insulin pump or multiple daily injections for bolus insulin.

*$p < .01$.

**$p < .001$.

TABLE 3. Eating Events and Insulin Restriction by Time of Day for 72 Hours of Momentary (Real-Time) Assessment

Time of Day	No. Individuals Reporting Eating	Total No. Eating Episodes	No. Individuals Reporting Insulin Restriction	Total No. Insulin Restriction Episodes	% of Eating Episodes with Insulin Restriction	% of Eating Episodes with Insulin Restriction, M (SD)
Morning (6:00–8:59 AM)	*n* = 34	60	*n* = 3	3	.05%	6% (0.2)
6:00–6:59 AM	*n* = 7	7	*n* = 0	0	0%	0% (0.0)
7:00–7:59 AM	*n* = 13	19	*n* = 1	1	5%	8% (0.3)
8:00–8:59 AM	*n* = 24	34	*n* = 2	2	6%	6% (0.2)
Midmorning (9:00–11:59 AM)	*n* = 46	80	*n* = 11	16	20%	16% (0.3)
9:00–9:59 AM	*n* = 30	36	*n* = 6	6	17%	18% (0.4)
10:00–10:59 AM	*n* = 17	19	*n* = 4	4	21%	21% (0.4)
11:00–11:59 AM	*n* = 21	25	*n* = 4	6	24%	17% (0.4)
Afternoon (12:00–2:59 PM)	*n* = 49	120	*n* = 14	24	20%	21% (0.4)
12:00–12:59 PM	*n* = 35	57	*n* = 6	8	14%	16% (0.4)
1:00–1:59 PM	*n* = 32	42	*n* = 7	11	26%	22% (0.4)
2:00–2:59 PM	*n* = 16	21	*n* = 4	5	24%	22% (0.4)
Late afternoon (3:00–5:59 PM)	*n* = 43	85	*n* = 15	24	28%	24% (0.4)
3:00–3:59 PM	*n* = 21	24	*n* = 6	7	29%	29% (0.5)
4:00–4:59 PM	*n* = 25	30	*n* = 8	9	30%	28% (0.4)
5:00–5:59 PM	*n* = 26	31	*n* = 7	8	26%	23% (0.4)
Evening (6:00–8:59 PM)	*n* = 50	105	*n* = 16	19	18%	22% (0.4)
6:00–6:59 PM	*n* = 28	38	*n* = 6	6	16%	18% (0.4)
7:00–7:59 PM	*n* = 30	36	*n* = 7	7	19%	18% (0.4)
8:00–8:59 PM	*n* = 24	31	*n* = 6	6	19%	23% (0.4)
Late evening (9:00–11:59 PM)	*n* = 34	57	*n* = 9	12	21%	23% (0.4)
9:00–9:59 PM	*n* = 19	23	*n* = 5	6	26%	26% (0.5)
10:00–10:59 PM	*n* = 18	24	*n* = 5	5	21%	21% (0.4)
11:00–11:59 PM	*n* = 10	10	*n* = 1	1	10%	10% (0.3)
Overnight (12:00–5:59 AM)	*n* = 12	18	*n* = 5	5	28%	32% (0.4)
12:00–12:59 AM	*n* = 6	8	*n* = 2	2	25%	25% (0.4)
1:00–1:59 AM	*n* = 4	4	*n* = 1	1	25%	25% (0.5)
2:00–2:59 AM	*n* = 2	2	*n* = 0	0	0%	0% (0.0)
3:00–3:59 AM	*n* = 3	3	*n* = 2	2	67%	67% (0.6)
4:00–4:59 AM	*n* = 0	0	*n* = 0	0	—	—
5:00–5:59 AM	*n* = 1	1	*n* = 0	0	0%	0% (0.0)

M (SD) = mean (standard deviation).

Average percentage of eating episodes with insulin restriction was calculated using each individual's percentage of insulin restriction for that time block and averaging across individuals.

Frequency of insulin restriction was correlated with metabolic control (total frequency and as percentage of meals/snacks consumed) (Table 2). After accounting for control variables, frequency of insulin restriction for meals predicted 27.2% of the variance in HbA_{1c}; an additional 7.9% of variance in HbA_{1c} was predicted by snack insulin restriction frequency ($F(4, 50) = 9.91$, $p < .001$). The variance in HbA_{1c} that was accounted for by the frequency of insulin restriction for 28 days (calculated as a percentage of meals and snacks consumed) was similar to the variance in HbA_{1c} accounted for by the frequency of insulin restriction during the 72 hours of real-time reporting (35% versus 34%, respectively).

DISCUSSION

The current study examined the frequency of restriction of short-acting insulin among individuals with T1D and eating disorder symptoms by time of day. Overall frequency of insulin restriction among participants was highly variable, with a few individuals restricting short-acting insulin at every meal/snack and others reporting this behavior far less frequently, or not at all. On average, T1D patients restricted insulin for 19% of the meals and snacks that they consumed for 72 hours of real-time reporting, and for 30% of meals/snacks reportedly consumed for the past 28 days. Participants' insulin restriction frequencies during the real-time assessment correlated with their report of the past 28 days (medium to large effect).

Frequency of insulin restriction varied by time of day and was least likely in the morning hours. Additional research is needed to determine whether eating early (6:00–8:59 AM) can help patients establish healthier patterns of insulin dosing throughout the day.

Insulin restriction was more common for meals/snacks consumed in the afternoon between 3:00 and 5:59 PM and peaked at 29% between 3:00 and 3:59 PM. This suggests that additional

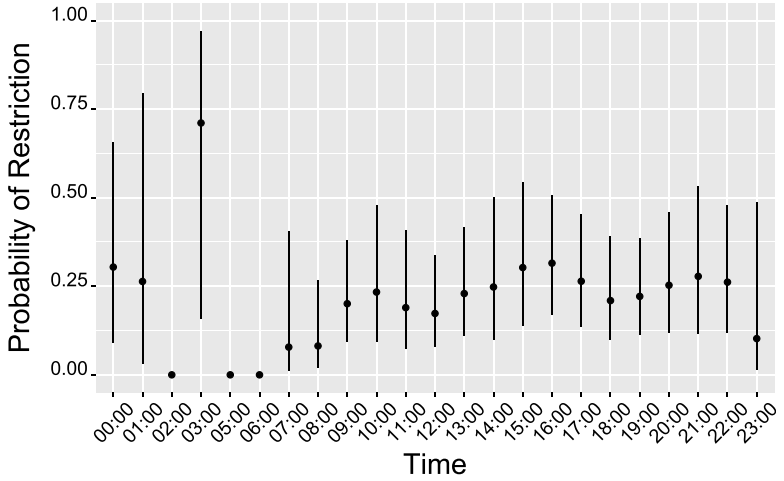

FIGURE 1. Insulin restriction by hour of day. Values are predicted probabilities with 95% confidence intervals.

therapeutic support at this time of day might be beneficial to patients with T1D with eating disorder symptoms. Results also suggest the need for research investigating why diabetes management becomes especially challenging in the late afternoon. Possible factors include calorie restriction earlier in the day that leads to overeating later, differences in the nutritional content or less structure for meals and snacks later in the day or the possibility that patients are more likely to experience low energy or mood at this time.

Insulin was also more likely to be restricted when individuals ate overnight (e.g., 12:00–6:00 AM; this does not include eating without giving insulin to correct hypoglycemia). However, eating overnight was rare, which is reported only 18 times during the 72-hour assessment by 5 individuals (3.4% of the total eating episodes reported).

Although eating overnight was uncommon, it may be important to identify this behavior in patients because it might contribute to hyperglycemia and could influence eating patterns and metabolic control into the next day (15). Many patients might not disclose eating during the night because of guilt or shame. Thus, it may be important for clinicians to ask directly about this behavior and in a nonjudgmental, matter-of-fact manner. Interventions to address insulin restriction for overnight eating might include eating more during the day or preparing a low-carbohydrate snack in advance for nocturnal consumption.

Participants more commonly restricted insulin for snacks than meals. Although restricting insulin for snacks may be less biologically impactful (accounting for an additional 8% of unique variance in HbA_{1c} relative to the 27% accounted for by mealtime insulin restriction), decreasing insulin restriction for snacks could produce clinically relevant reductions in HbA_{1c}.

There are several possible reasons that individuals might restrict insulin more frequently for snacks than meals: Snacks might be less likely to be planned. Thus, individuals may be less prepared or less willing to give insulin. Individuals might also be better able to self-justify not giving insulin for snacks than for meals or have less support or accountability at snack times (e.g., snacks may be more likely to be eaten alone). In an earlier report, we found that "breaking a personal dietary rule" was associated with significantly greater odds of insulin restriction for that eating episode (8). Thus, it could be that individuals are more likely to eat foods that they consider "off limits" between meals (e.g., cookies, cakes, chips) and then restrict insulin to negate the potential weight gain associated with consumption of high-calorie food.

As expected, greater frequency of insulin restriction was associated with poorer metabolic control during the immediate postprandial period. The impact of insulin restriction on metabolic control was also reflected in higher average of blood glucose (as indexed by CGM and HbA_{1c}). These results highlight the clinical importance of insulin restriction and suggest that participants' self-reports of insulin restriction correspond with real-world behaviors and outcomes.

The variability in frequency of insulin restriction in this sample of T1D patients points to the continuum of symptom severity and variation in clinical presentation among patients with T1D who screen positive for eating disorder symptoms. Future research should determine how best to identify patients for whom intentional insulin restriction for weight loss is a central issue. Studies might also identify factors that distinguish patients who omit insulin from those who do not (i.e., risk or vulnerability factors) and whether patients with T1D who purge via insulin restriction require a different intervention strategy than those who report uncontrolled eating or distorted body image but do not restrict insulin.

Limitations

The current study had limitations worth noting. The assessment method had some clear strengths but also weaknesses. The momentary, real-time assessment may have been subject to experimental reactivity. That is, participants may have altered behavior because they were reporting it in real time. This may have resulted in either an increase or a decrease in insulin restriction observed for 72 hours. The interview may have also been subject to demand characteristics (with participants over or under reporting based on what they perceived to be desirable) and the biases of retrospective recall, including primacy and recency effects. Although the momentary and interview insulin restriction frequencies were correlated, participants reported restricting insulin for a greater percentage of meals for the past 28 days than was observed in the real-time assessment. This might suggest that the 72-hour assessment was not long enough to capture

TABLE 4. Eating Events and Insulin Restriction by Meal Type for 28 Days of Retrospective Recall

Meal/Snack	No. Individuals Reporting Eating	Total No. Eating Episodes	No. Individuals Restricting Insulin	Total No. Insulin Restriction Episodes	% of Eating Episodes with Insulin Restriction	No. Times Meal/Snack Consumed for 28 d, M (SD)	No. Times Insulin Restricted for 28 d, M (SD)	% of Eating Episodes with Insulin Restriction, M (SD)
Breakfast	*n* = 56	1222	*n* = 26	226	18%	20.7 (9.5)	3.9 (6.5)	23% (33.4)
Midmorning Snack	*n* = 48	566	*n* = 28	207	37%	9.6 (8.3)	3.6 (5.7)	42% (43.6)
Lunch	*n* = 59	1415	*n* = 38	287	20%	24.0 (6.3)	5.00 (5.9)	23% (27.1)
Afternoon Snack	*n* = 57	948	*n* = 39	469	49%	16.1(9.2)	8.1 (8.8)	50% (41.1)
Dinner	*n* = 59	1528	*n* = 38	361	24%	25.9 (4.9)	6.2 (7.9)	24% (28.8)
Evening snack	*n* = 55	1060	*n* = 33	408	38%	18.0 (9.2)	7.0 (8.7)	37% (37.9)
Nocturnal Eating	*n* = 13	88	*n* = 8	51	58%	1.5 (4.0)	0.9 (3.0)	58% (49.4)

M (SD) = mean (standard deviation).

Average percentage of eating episodes with insulin restriction was calculated using each individual's percentage of insulin restriction for that time block and averaging across individuals. Nocturnal eating does not include waking and consuming carbohydrate due to hypoglycemia.

typical patterns of behavior or a memory bias in the interviews to recall restriction of insulin.

In the current study, participants did not provide additional information about the situational or emotional factors influencing their decision to restrict insulin in the moment. This is a limitation of the current study and a direction for future research. Future studies might also replicate these findings with an objective measure of insulin restriction. However, this would necessitate synthesizing insulin pump data, detailed dietary records, planned and actual activity levels, potential illness, carb-insulin ratio instruction, and blood sugar level and trend at time of eating. Gathering information on diet and exercise could be particularly challenging for individuals with eating and weight concerns and introduce additional experimental reactivity. In addition, only a subset of patients uses insulin pumps. Thus, an objective measure of insulin restriction, while ideal, poses challenges.

The current study did not differentiate complete omission of insulin from partial restriction of insulin (or underdosing), nor did it examine restriction of long-acting insulin. Future studies may find that these are meaningful distinctions, and the factors that influence complete and partial restriction or restriction of short versus long-acting insulin are different and require different intervention strategies.

There may be limitations to the generalizability of the findings. The sample was self-selected for interest in eating and weight concerns in T1D. The sample was also predominately female (93%). Although this is expected given that females are at higher risk for eating disorders (16), findings are not necessarily generalizable beyond this sample of fairly well-educated women with T1D. There are also individual differences in diurnal rhythms, and the data were not adjusted for individual waking times.

In conclusion, the current study is the first study to describe the frequency and time-of-day distribution of insulin restriction events among individuals with T1D and eating disorder symptoms. Our findings highlight variability in this behavior among patients and suggest late afternoon as a possible opportunity for additional therapeutic support and behavior change. They also highlight the potential relevance of inquiring about overnight eating, which, if present, may have a high likelihood of insulin restriction and destabilize metabolic control. In addition to suggesting key times for intervention, these results may inform additional research to identify relevant contextual variables for insulin restriction that may further inform treatment strategies for this high-risk patient population.

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