**Supplemental Table S1. HbA1c, CGM Average Glucose Levels, Time-in-Range and Glucose Coefficients of Variation in the NA and IAH Cohorts**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Total (n=115) | NA (n=50) | IAH (n=49) |
| HbA1c, % (mmol/mol) | 7.4±1.2 (57.4) | 7.5±1.5 (58.5) | 7.3±0.8 (56.3) |
| CGM average glucose level, mg/dL | | | |
| Total | 161±34 | 161±37 | 162±31 |
| Day | 162±35 | 161±38 | 162±31 |
| Night | 161±38 | 161±41 | 161±36 |
| CGM glucose time-in-range, % | | | |
| Total | 63.6±18.5 | 65.3±20.4 | 62.0±16.2 |
| Day | 63.6±18.4 | 65.4±20.4 | 61.9±16.0 |
| Night | 63.7±21.0 | 65.1±23.1 | 62.2±18.6 |
| CGM glucose coefficient of variation, % | | | |
| Total | 35.3±6.6 | 33.3±6.0 | 37.4±6.6 |
| Day | 34.8±6.7 | 32.9±6.2 | 36.8±6.6 |
| Night | 34.6±7.8 | 32.0±6.8 | 37.2±7.9 |

Data presented in mean±standard deviation. HbA1c, hemoglobin A1C; CGM, continuous glucose monitoring; NA, normal awareness; IAH, impaired awareness of hypoglycemia.

**Supplemental Table S2. Total Hypoglycemia Duration and AUCs over Two-week Period**

|  |  |  |  |
| --- | --- | --- | --- |
|  | NA | IAH | *P*-value |
| Duration with glucose <70 mg/dL, minute | | | |
| Total | 293 (85.0, 719) | 445 (272.5, 1223) | 0.010 |
| Day | 185 (58.8, 429) | 335 (113, 720) | 0.033 |
| Night | 85 (30.0, 234) | 195 (45.0, 528) | 0.008 |
| Duration with glucose <54 mg/dL, minute | | | |
| Total | 35 (0, 146) | 125 (35.0, 318) | 0.003 |
| Day | 12.5 (0, 92.5) | 70 (12.5, 183) | 0.027 |
| Night | 0 (0, 41.3) | 35.0 (7.5, 105) | 0.002 |
| AUC with glucose <70 mg/dL, minute\*mg/dL | | | |
| Total | 2535 (500, 6695) | 5060 (2185, 15810) | 0.004 |
| Day | 1568 (359, 4314) | 3110 (1003, 8258) | 0.016 |
| Night | 493 (125, 2420) | 2180 (530, 5315) | 0.003 |
| AUC with glucose <54 mg/dL, minute\*mg/dL | | | |
| Total | 160 (0, 926) | 770 (188, 2233) | 0.002 |
| Day | 47.5 (0, 765) | 375 (35.0, 1298) | 0.020 |
| Night | 0 (0, 271) | 210 (20.0, 663) | 0.001 |

Data presented in median (interquartile range) and analyzed by Mann-Whitney test. AUC, area under the curve calculated by formula (hypoglycemia threshold – continuous glucose monitoring glucose value) x five minutes for each glucose point during hypoglycemia; NA, normal awareness; IAH, impaired awareness of hypoglycemia.

**Supplemental Table S3. Prolonged Hypoglycemic Events1 in NA/IAH Groups**

|  |  |  |  |
| --- | --- | --- | --- |
| Participant ID | Time (minute) | AUC  (minute\*mg/dL) | Day (D)/night (N) time2 |
| NA Group | | | |
| 16 | 190 | 1815 | N |
| 140 | 150 | 2005 | D |
| 181 | 135 | 635 | D |
| IAH Group | | | |
| 5 | 120 | 1260 | N |
| 5 | 215 | 2275 | D |
| 5 | 315 | 3290 | D |
| 29 | 295 | 2655 | N |
| 48 | 125 | 1625 | N |
| 48 | 140 | 910 | N |
| 48 | 165 | 675 | D |
| 48 | 180 | 985 | D |
| 48 | 185 | 2490 | D |
| 48 | 200 | 2400 | N |
| 48 | 380 | 2940 | D |
| 52 | 155 | 1080 | N |
| 52 | 165 | 1640 | N |
| 52 | 350 | 4695 | N |
| 78 | 120 | 1365 | D |
| 106 | 130 | 1645 | D |
| 113 | 150 | 1060 | N |
| 113 | 155 | 1330 | D |
| 113 | 180 | 2040 | D |
| 113 | 185 | 2270 | N |
| 113 | 190 | 2030 | D |
| 118 | 225 | 1705 | N |
| 145 | 130 | 975 | D |
| 145 | 185 | 1730 | D |
| 155 | 145 | 1905 | D |
| 155 | 525 | 7280 | N |

NA, normal awareness; IAH, impaired awareness of hypoglycemia; AUC, area under the curve calculated by formula (54 – CGM value) x five minutes for each glucose point during a hypoglycemic event; CGM, continuous glucose monitoring.

1A prolonged hypoglycemic event was defined by CGM glucose <54 mg/dL for consecutive 120 minutes or more.

20600-2200 of CGM time was considered to be the day time; 2201-0559 was considered to be the night time. A hypoglycemic event is considered to be day/night-time based on the timing of the first glucose below the hypoglycemia threshold.

**Supplemental Table S4. Hypoglycemic Event Numbers with the 15-minute Criterion**

|  |  |  |  |
| --- | --- | --- | --- |
|  | NA | IAH | *P*-value |
| Event number with glucose <70 mg/dL lasting ≥15 minutes1, n | | | |
| Total | 6 (3, 13) | 9 (6, 17) | **0.025** |
| Day | 4 (1, 9) | 7 (3, 12) | 0.084 |
| Night | 2 (1, 4) | 3 (1, 6) | **0.010** |
| Event number with glucose <54 mg/dL lasting ≥15 minutes1, n | | | |
| Total | 1 (0, 3) | 3 (1, 6) | **0.006** |
| Day | 1 (0, 3) | 2 (0, 5) | **0.012** |
| Night | 0 (0, 1) | 1 (0, 2) | **0.043** |

Data presented in median (interquartile range) and analyzed by Mann-Whitney test. Boldface indicates statistical significance. NA, normal awareness; IAH, impaired awareness of hypoglycemia.

1The 15-minute criterion is met with at least three consecutive glucose values with five-minute intervals being below the hypoglycemia threshold.

**Supplemental Table S5. Logistic Regression Model on Hypoglycemia Metrics between NA and IAH Patients adjusted for CGM Use Duration**

|  |  |  |
| --- | --- | --- |
|  | **Odds Ratio** | **95%CI** |
| Percentage of CGM values <70 mg/dL | | |
| Total | 1.11 | 1.00 – 1.27 |
| Day | 1.09 | 0.99 – 1.24 |
| Night | 1.12 | 1.01 – 1.26 |
| Percentage of CGM values <54 mg/dL | | |
| Total | 1.50 | 1.08 – 2.41 |
| Day | 1.41 | 1.03 – 2.19 |
| Night | 1.34 | 1.04 – 1.95 |
| Event number with glucose <70 mg/dL, n | | |
| Total | 1.03 | 0.99 – 1.08 |
| Day | 1.02 | 0.97 – 1.09 |
| Night | 1.18 | 1.02 – 1.38 |
| Event number with glucose <54 mg/dL, n | | |
| Total | 1.09 | 1.00 – 1.19 |
| Day | 1.10 | 0.98 – 1.25 |
| Night | 1.26 | 1.01 – 1.62 |
| Event duration with glucose <70 mg/dL, minute | | |
| Total | 1.03 | 1.01 – 1.07 |
| Day | 1.04 | 1.00 – 1.09 |
| Night | 1.06 | 1.01 – 1.12 |
| Event duration with glucose <54 mg/dL, minute | | |
| Total | 1.10 | 1.02 – 1.20 |
| Day | 1.12 | 1.01 – 1.27 |
| Night | 1.19 | 1.03 – 1.47 |
| Event number with glucose <70 mg/dL lasting ≥20 minutes1, n | | |
| Total | 1.05 | 0.99 – 1.11 |
| Day | 1.05 | 0.98 – 1.14 |
| Night | 1.19 | 1.00 – 1.43 |
| Event number with glucose <54 mg/dL lasting ≥20 minutes1, n | | |
| Total | 1.14 | 1.01 – 1.35 |
| Day | 1.24 | 1.02 – 1.57 |
| Night | 1.19 | 0.90 – 1.64 |

CGM, continuous glucose monitoring system; NA, normal awareness; IAH, impaired awareness of hypoglycemia; 95%CI, 95% confidence interval.

1The 20-minute criterion is met with at least four consecutive glucose values with five-minute intervals being below the hypoglycemia thresholds.

**Supplemental Figure S1.** Bar graphs showing the distributions of continuous glucose monitoring systems used by patients with NA, undetermined and IAH status. The hypoglycemia awareness status was determined by the Clarke questionnaire. *NA, normal awareness; IAH, impaired awareness of hypoglycemia.*

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**Supplemental Figure S2.** Histogram by the Clarke score for the relative frequencies of all study participants (N=115). Numbers above each bar represent the number of participants with the Clarke score.

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