Insulin-associated weight gain in Type 2 Diabetes Mellitus is associated with increases in sedentary behavior

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The insulin therapy-mediated weight gain in patients with type 2 diabetes (T2D) may relate to altered physical activity patterns (1). In this study, we examined the hypothesis that initiation of insulin therapy would be associated with an increase sedentary behavior (i.e. sitting time) and lower low-, moderate- and vigorous-intensity physical activity, which subsequently relate to weight gain.

We included 40 T2D patients who started insulin therapy, who were followed for a period of 12-months. Patients were randomly selected from one university hospital, three non-university teaching hospitals and four primary care practices. The decision to start insulin treatment was at the discretion of the responsible physician and was always based on failure of glycemic control while on oral glucose-lowering agents and diet. Measurements were performed before, 6-months and 12-months after initiation of insulin therapy. We examined body weight, waist/hip-circumference, fasting glucose, and HbA1c using standardized procedures. Free-living daytime physical activity was objectively measured (SenseWear Pro3 Armband™, Body Media, Pittsburgh, PA, USA) (2). We examined: *1.* Time (hours/day) spent in sitting (<1.5METs), low intensity physical activity (LPA, 2.1-3.0METs), and moderate-to-vigorous physical activity (MVPA, >3.0METs), *2.* Steps per day, and *3.* Sit-to-stand maneuvers (transition from ≥5-minutes sitting to LPA).

Across 12-months, body weight increased 2.9±4.5kg ($P<0.05$). This observation is largely in line with earlier findings (3). Furthermore, fasting glucose and HbA1c decreased across 12-months (both $P<0.05$). Interestingly, we found an increase in sitting time and a decrease in LPA, but no change in MVPA (Figure 1A-C). Number of steps (7854±3936 to 6060±3022) and sit-to-stand maneuvers (20±5 to 18±6) significantly decreased (both $P<0.05$). These findings show an increase in sedentary behavior, rather than a decrease in physical activity

(including exercise time), that occurs simultaneously with an increase in body weight after initiation of insulin therapy. Since sedentary behavior replaced LPA, lower energy expenditure may relate to our observation (4). However we found no relation between changes in energy expenditure and weight gain (r=-0.195, P=0.227). Excessive caloric intake less likely explains our observation, since food diaries revealed no increase in caloric intake (1721±839 to 1460±367, P=0.074).

T2D patients with BMI<30kg/m^2 (64±10 years) showed less sitting time (P=0.012) and more LPVA (P=0.012) than those with BMI≥30kg/m^2 (57±9 years). Surprisingly, upon insulin therapy, BMI and waist circumference increased in subjects with BMI<30kg/m^2, but not in BMI≥30kg/m^2. Similarly, patients with BMI<30kg/m^2, but not with BMI≥30kg/m^2, demonstrated an increase in sitting time and a decrease in energy expenditure and steps/day (data not shown). We found significant, positive relations between changes in weight and waist circumference *versus* sitting time (Figure 1D-E). This fits with previous work in non-diabetic populations, where an increase in sedentary behavior was related to weight gain (5). T2D patients with BMI≥30kg/m^2 did not demonstrate these relations (r=-0.186 and -0.041, P=0.474 and 0.879, respectively). A potential explanation for these unexpected between-groups differences may relate to a ceiling effect in sedentary behavior in patients with BMI ≥30kg/m^2. Indeed, the average sitting time of 12.5-h makes it practically difficult to further increase sedentary behavior.

We observed that the initiation of insulin therapy was associated with an increase in sedentary behavior and limited changes in MVPA. This suggests that increased sedentary behavior, especially in non-obese T2DM patients, may contribute to body weight gain after initiation of

insulin therapy. These findings suggest that sedentary behavior assessment and intervention may be needed in T2D management.

ARTICLE INFORMATION

Duality of interest

No conflicts of interest, financial or otherwise, are declared by the author(s).

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Author contributions

YH was responsible for data analysis, drafted the first manuscript, performed and interpreted statistical analysis. HJJ contributed to data collection. MTEH performed and interpreted statistical analysis. CJT devised and designed the experiment, arranged funding, and performed and interpreted statistical analysis. DHT devised and designed the experiment, arranged funding, performed and interpreted statistical analysis. All authors have contributed to writing of the manuscript and provided approval of the final version.

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FIGURE LEGEND

FIGURE 1. A-C: Physical activity patterns in T2D patients at baseline (T0) and after 6 (T6) and 12 months (T12) of the start of insulin therapy, where patterns are presented as sitting (h/day, A), low-intensity physical activity (LPA in h/day, B) and moderate-to-vigorous physical activity (MVPA in h/day, C). The plot elements are presented as follows: the length of the box represents the interquartile range (the distance between the 25^{th} and the 75^{th} percentiles), the horizontal line in the box interior represents the median, and the vertical lines issuing from the box extend to the minimum and maximum values of the variables. *Post-hoc significantly different from T0 at $P<0.05$. D,E: Spearman correlations of change in sitting time between baseline and 12 months of insulin therapy and weight gain (D) and waist circumference (E) among T2D patients with baseline BMI $<30 kg/m^2$. Spearman rank correlation coefficients (r) are shown for each correlation. Solid lines indicate linear regression function.

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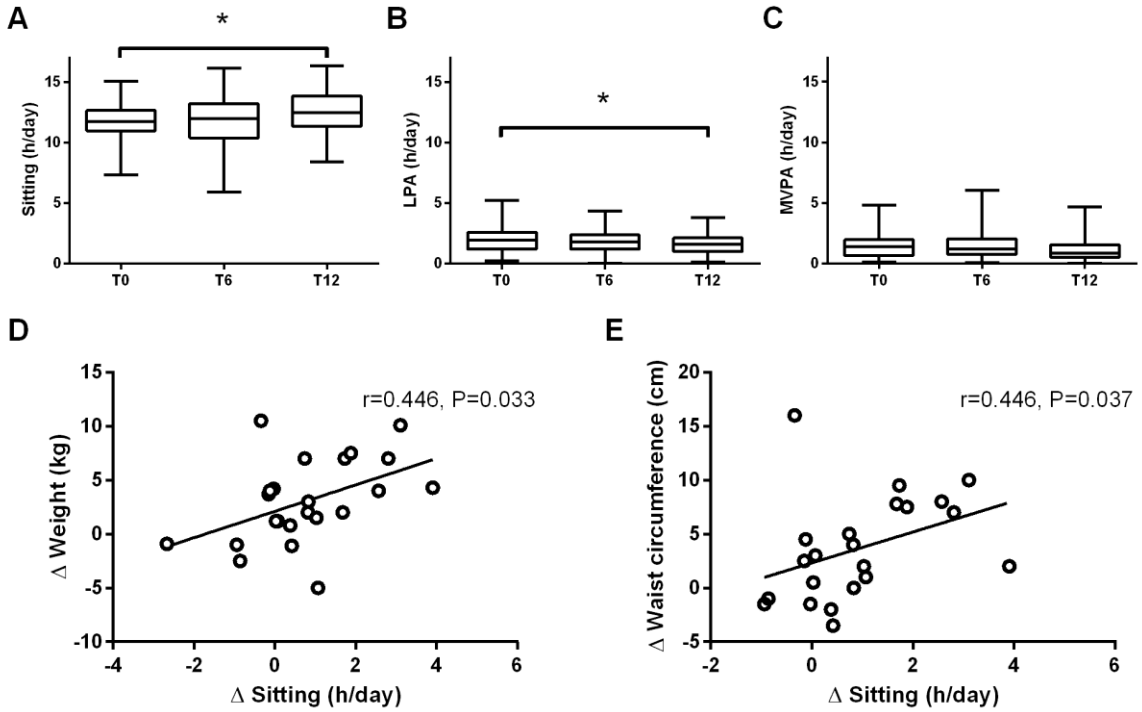
A
*
Sitting (h/day)
15
10
5
0
T0
T6
T12
B
*
LPA (h/day)
15
10
5
0
T0
T6
T12
C
MVPA (h/day)
15
10
5
0
T0
T6
T12
D
r=0.446, P=0.033
Δ Weight (kg)
15
10
5
0
-5
-10
-4
-2
0
2
4
6
Δ Sitting (h/day)
E
r=0.446, P=0.037
Δ Waist circumference (cm)
20
15
10
5
0
-5
-2
0
2
4
6
Δ Sitting (h/day)