Exercise Therapy in Type 2 Diabetes

Is daily exercise required to optimize glycemic control?

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OBJECTIVE—Given the transient nature of exercise-induced improvements in insulin sensitivity, it has been speculated that daily exercise is preferred to maximize the benefits of exercise for glycemic control. The current study investigates the impact of daily exercise versus exercise performed every other day on glycemic control in type 2 diabetic patients.

RESEARCH DESIGN AND METHODS—Thirty type 2 diabetic patients (age 60 ± 1 years, BMI 30.4 ± 0.7 kg/m^2, and HbA_{1c} 7.2 ± 0.2%) participated in a randomized crossover experiment. Subjects were studied on three occasions for 3 days under strict dietary standardization but otherwise free-living conditions. Blood glucose homeostasis was assessed by continuous glucose monitoring over 48 h during which subjects performed no exercise (control) or 60 min of cycling exercise (50% maximal workload capacity) distributed either as a single session performed every other day or as 30 min of exercise performed daily.

RESULTS—The prevalence of hyperglycemia (blood glucose >10 mmol/L) was reduced from 7:40 ± 1:00 h:min per day (32 ± 4% of the time) to 5:46 ± 0:58 and 5:51 ± 0:47 h:min per day, representing 24 ± 4 and 24 ± 3% of the time, when exercise was performed either daily or every other day, respectively ($P < 0.001$ for both treatments). No differences were observed between the impact of daily exercise and exercise performed every other day.

CONCLUSIONS—A short 30-min session of moderate-intensity endurance-type exercise substantially reduces the prevalence of hyperglycemia throughout the subsequent day in type 2 diabetic patients. When total work is being matched, daily exercise does not further improve daily glycemia compared with exercise performed every other day.

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The level of glycemia (1,2), and particularly postprandial glycemia (3–5), has been associated with the development of cardiovascular complications in type 2 diabetes. Therefore, glycemic control is fundamental to type 2 diabetes treatment. Since the effects of structured exercise training on glycemic control have been well established (6), exercise is considered a cornerstone in type 2 diabetes treatment.

A single bout of exercise lowers circulating blood glucose concentrations and reduces the prevalence of hyperglycemic episodes throughout the subsequent day in type 2 diabetic patients (7–9). These glucoregulatory properties of exercise are attributable to an increase in whole-body insulin sensitivity, which has been reported to persist for up to 48 h following a single bout of exercise (10–12). As such, the benefits of exercise on long-term glycemic control (i.e., HbA_{1c}) can be largely ascribed to the cumulative glucoregulatory effects of each successive bout of exercise, rather than the structural adaptive response to prolonged exercise training (10,11). In fact, the effects of more prolonged exercise training on insulin sensitivity may be lost entirely 6–8 days after cessation of training (13,14). Therefore, regular exercise is warranted to improve and/or maintain long-term glycemic control. This is also recognized by the recently updated exercise guidelines of the American College of Sports Medicine and the American Diabetes Association (15), which state that exercise should be performed at least 3 days/week with no more than two consecutive days between exercise bouts.

Given the short-lived character of exercise-induced improvements in insulin action, it has even been speculated that daily exercise would be the preferred frequency of exercise to improve glycemic control in type 2 diabetes (11,16). However, since most exercise intervention studies typically divided the total amount of exercise over three exercise sessions per week (17), it is presently unclear whether daily exercise sessions provide an equal or additional benefit with respect to glycemic control compared with a less frequent exercise regimen. Moreover, shorter daily exercise sessions may be preferred over less frequent bouts of a longer duration in more compromised type 2 diabetic patients. These patients are commonly characterized by a high prevalence of cardiovascular comorbidities, polyneuropathy, and/or reduced exercise tolerance, which generally reduce the capacity to perform more prolonged bouts of exercise. More information on the preferred frequency of exercise would provide health care professionals with a useful instrument to individualize and, as such, optimize exercise intervention programs to treat type 2 diabetes.

The current study investigates the impact of daily exercise versus exercise performed every other day on glycemic control throughout the day in insulin-treated and non–insulin-treated type 2 diabetic patients. For this purpose, we applied continuous glucose monitoring under standardized dietary, but otherwise free-living, conditions over a 48-h period during which patients performed no exercise (control) or 60 min of cycling exercise distributed either as a single session performed every other day (nondaily) or as 30 min of exercise performed daily (daily). We hypothesized that daily exercise improves blood glucose homeostasis to a greater extent compared with the same amount of exercise performed every other day.

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RESEARCH DESIGN AND METHODS

—Thirty male type 2 diabetic patients were recruited to participate in a randomized crossover study. Both non–insulin-treated (n = 16) and insulin-treated (n = 14) type 2 diabetic patients were selected. Exclusion criteria were self-reported renal failure and liver disease (hepatitis and cirrhosis), morbid obesity (BMI >40 kg/m^2), uncontrolled hypertension (>160 mmHg systolic and/or >100 mmHg diastolic blood pressure), and a history of severe cardiovascular problems (myocardial infarction in the last year or stroke). All subjects were informed of the nature and the risks of the experimental procedures before their written informed consent was obtained. The medical ethics committee of the Maastricht University Medical Centre+ approved all clinical experiments.

Screening and pretesting

Non–insulin-treated patients performed an oral glucose tolerance test (OGTT). Blood glucose–lowering medication was withheld 2 days prior to the OGTT. After an overnight fast, subjects arrived at the laboratory at 8:00 A.M. by car or public transportation. A fasting blood sample was obtained, after which the OGTT was performed to determine type 2 diabetes according to the American Diabetes Association criteria (18). Insulin-treated type 2 diabetic patients were screened with a basal blood sample to determine their fasting plasma glucose concentration and HbA_{1c} level. After blood sampling, maximal workload capacity (W_{max}) was determined with an electromagnetically braked cycle ergometer (Lode Excalibur, Groningen, the Netherlands) during an incremental exhaustive exercise test. Cardiac function was monitored using a 12-lead electrocardiogram.

Study design

Subjects participated in a randomized crossover study consisting of three intervention periods separated by at least 4 days. Each intervention period consisted of 3 days during which the impact of moderate-intensity cycling exercise (50% W_{max}) on 48-h blood glucose homeostasis was assessed under standardized dietary, but otherwise free-living, conditions (Fig. 1). All intervention periods were identical with the exception of the frequency and duration of the exercise sessions. During one intervention period (nondaily), a single 60-min bout of exercise was performed at the beginning of the 48-h assessment. In the other intervention period (daily), the same amount of exercise was performed via two exercise sessions of 30 min each. The first 30-min session was performed at the beginning of the 48-h assessment and the second session exactly 24 h later. In a third intervention period (control), subjects performed no exercise at all.

On day 1 of each intervention period, subjects arrived at the laboratory at 7:30 A.M. after an overnight fast. A continuous glucose-monitoring device (GlucoDayS; A. Menarini Diagnostics, Firenze, Italy) was attached, and subjects received a short training in capillary blood sampling (Glucocard X Meter; Arkray, Kyoto, Japan). After breakfast at 8:30 A.M., the exercise session was started at 10:00 A.M. for both exercise treatments. At 11:15 A.M., subjects were free to go home and resume their normal daily activities. On day 2, subjects reported to the laboratory at 8:00 A.M. After breakfast at 8:30 A.M., the exercise session was started at 10:00 A.M. (only for the daily exercise experiment). In case no exercise was performed at 10:00 A.M., subjects were rested in a chair. At 11:15 A.M., subjects were free to go home and resume their normal daily activities. On days 1 and 2, venous blood samples were obtained in fasting conditions (at 8:15 A.M.) and 2.5 h following breakfast (at 11:00 A.M.). On day 3, subjects arrived at the laboratory after 10:00 A.M. for removal of the continuous glucose-monitoring device (Fig. 1).

Exercise protocol

The exercise sessions consisted of either 30- or 60-min cycling at a constant workload (Lode Excalibur). The applied workload of 50% W_{max} was based on previous studies from our laboratory (19,20), which have shown that this workload can be maintained for 60 min by type 2 diabetic patients. In addition, these studies reported that a workload of 50% W_{max} corresponds with ~60% of patients' $V_{O_{2max}}$, with lactate concentrations remaining <4 mmol/L (ranging from ~2.5 to 3.5 mmol/L over the 60-min course of exercise [19,20]). Consequently, we assumed that patients in the current study would exercise below their anaerobic threshold.

Diet and physical activity

All subjects were asked to maintain their habitual physical activity patterns throughout the experimental period but to refrain from exhaustive physical labor and exercise training for 2 days prior to and during the experimental period. During the experimental periods, physical activity was assessed using a validated triaxial accelerometer (Philips DirectLife, Eindhoven, the Netherlands) (21), worn in a belt around the waist. Total physical activity, including exercise, was determined by the sum of accelerometer counts obtained over the 48-h assessment periods. Non–exercise-associated physical activity was determined in a similar fashion after discarding the time periods between 10:00 and 11:00 A.M. on days 1 and 2 (time of exercise treatment) in all experimental periods.

During each experimental period, subjects were provided with a healthy standardized diet, composed according to the American Diabetes Association dietary recommendations for type 2 diabetes (22). The diet consisted of three meals and three snacks per day, distributed in preweighed packages and ingested at predetermined time points to ensure a fully standardized diet. The diet provided 10.3 ± 0.1 MJ/day consisting of 55% of energy from carbohydrate, 14% from protein, and 31% from fat. The diet was designed to meet the individual energy requirements as calculated with the Harris and Benedict equation (1918) multiplied with a physical activity level value of 1.4. The resulting energy requirements represent a sedentary lifestyle.

Medication

Non–insulin-treated patients were treated with metformin only (n = 10), metformin combined with a sulfonylurea or thiazolidinedione (n = 5), or diet only (n = 1). Insulin-treated patients were treated with an insulin pump (n = 2) or basal (n = 1), biphasic (n = 3), or multiple (n = 8) insulin injection regimens, with (n = 11) or without (n = 3) combined use of oral blood glucose–lowering medication. Oral blood glucose–lowering medication and/or exogenous insulin treatment was continued as normal throughout the entire experimental period. Insulin-treated patients were explicitly asked not to deviate from their habitual exogenous insulin treatment schemes when exercise was performed.

Blood sample analysis

Venous blood samples (5 mL) were collected in EDTA-containing tubes and centrifuged at 1,000*g* and 4°C for 10 min. Aliquots of plasma were immediately frozen in liquid nitrogen and stored at −80°C until analyses. Plasma glucose concentrations

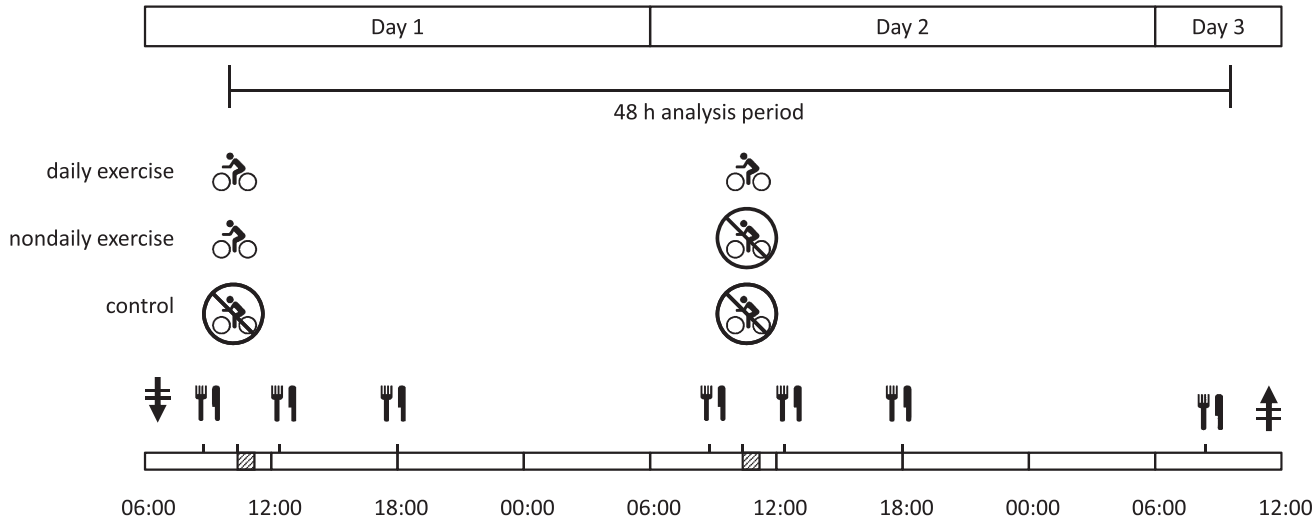

Figure 1—*Schematic overview of an experimental period. A continuous glucose-monitoring device was inserted (↡) at 7:30 A.M. on day 1 and removed (↟) after 10:00 A.M. on day 3. During an experimental period, subjects' blood glucose concentrations were monitored over a 48-h period during which subjects performed no exercise (control), or 60 min of cycling exercise (50% W_{max}), distributed either as a single session at the beginning of the monitoring period (nondaily) or as 30 min per day (daily). The exercise sessions (🚲) were initiated at 10:00 A.M. In case no exercise (🚫) was performed in the morning, subjects were resting in a chair. On days 1 and 2 of each experimental period, subjects consumed breakfast at the laboratory and were free to go home and resume their normal daily activities after 11:15 A.M. During an experimental period, subjects consumed a standardized diet with main meals (🍴) ingested at 8:30 A.M., 12:30 P.M., and 6:00 P.M.*

(Roche, Basel, Switzerland) were determined with a COBAS FARA semiautomatic analyzer (Roche). Insulin concentrations were determined by radioimmunoassay (Linco, St Charles, MO) and were only determined in the non–insulin-treated diabetic patients. HbA_{1c} content was determined by high-performance liquid chromatography (Bio-Rad Diamat, Munich, Germany).

Statistics and data analysis

The data obtained by the continuous glucose monitor were downloaded to a personal computer with GlucoDay software (V3.2.2). Values reported by the continuous glucose-monitoring device were converted into glucose values using the self-monitored capillary blood glucose values, which were obtained before each main meal and before the night. The glycemic profiles during the 48-h monitoring period (from 10:00 A.M. on day 1 to 10:00 A.M. on day 3) were used to determine average glucose concentrations, the prevalence of hyperglycemia (glucose concentrations >10 mmol/L), and the prevalence of hypoglycemia (glucose concentrations <3.9 mmol/L). Treatment effects were assessed by one-way repeated-measures ANOVA, with exercise treatment as within-subject factor. When applicable, pairwise comparisons with Bonferroni correction were applied to locate differences between interventions. Statistical comparisons were considered significant when P values were <0.05. All statistical calculations were performed using the SPSS 15.0.1.1 software package. Unless otherwise specified, shown results represent means ± SEM.

RESULTS—Subjects' characteristics are shown in Table 1. Insulin- and non–insulin-treated type 2 diabetic patients were comparable with respect to age, BMI, HbA_{1c}, and W_{max}. Non–insulin-treated patients had been diagnosed with type 2 diabetes for 5 ± 1 years, whereas insulin-treated patients had been diagnosed for 12 ± 2 years (P = 0.001) and had been treated with exogenous insulin for 5 ± 2 years.

Experimental periods

All 30 subjects successfully completed each of the three experimental treatments (control and daily and nondaily exercise). Subjects were compliant with respect to their medication and standardized diet, as verified by dietary records. Both dosing and timing of blood glucose–lowering medication were identical during the three experimental periods, since these factors were registered during the first experimental period and replicated during the second and third periods. During the experimental periods, insulin-treated patients were using 0.84 ± 0.11 units insulin/kg body wt/day.

Physical activity level

Total physical activity recorded over the 48-h period in both the daily and nondaily experimental conditions (2,467 ± 131 and 2,555 ± 121 kilocounts [kcounts], respectively) was higher when compared with the control experiment (2,304 ± 128 kcounts; main effect P = 0.004). However, non–exercise-associated physical activity in both the daily and nondaily experimental conditions (2,205 ± 121 and 2,307 ± 117 kcounts) did not differ compared with the control experiment (2,239 ± 128 kcounts; main effect P = 0.29).

Plasma glucose and insulin concentrations

Fasting plasma glucose and insulin concentrations assessed on the first day of each intervention period did not differ between treatments. Postbreakfast plasma glucose and insulin concentrations on day 1 showed a dose-dependent effect after performing 30 and 60 min of exercise, respectively (main effect P < 0.001 for both glucose and insulin) (Fig. 2). On the second day, fasting plasma glucose and insulin concentrations did not differ between treatments, indicating that a single bout of exercise performed on the previous day does not affect fasting plasma glucose and insulin concentrations. Postbreakfast plasma glucose and insulin concentrations on day 2 were lower in the daily exercise experiment compared with

Table 1—*Subjects' characteristics*

Group	Non–insulin treated	Insulin treated	*P*
n	16	14	
Age (years)	60 ± 2	60 ± 2	0.914
Time since diagnosis of type 2 diabetes (years)	5.0 ± 0.7	11.6 ± 1.9	0.001
Time on insulin therapy (years)	NA	5.1 ± 1.6	NA
BMI (kg/m^2)	29.8 ± 0.9	31.1 ± 1.0	0.337
HbA_{1c} (%)	7.0 ± 0.2	7.4 ± 0.2	0.227
HbA_{1c} (mmol/mol)	53 ± 2	57 ± 3	0.227
Fasting plasma glucose (mmol/L)	8.4 ± 0.5	8.0 ± 0.8	0.590
2-h postchallenge plasma glucose (mmol/L)	14.5 ± 1.0	NA	NA
Fasting plasma insulin (pmol/L)	137 ± 15	NA	NA
2-h postchallenge plasma insulin (pmol/L)	491 ± 118	NA	NA
OGIS index	272 ± 14	NA	NA
Systolic blood pressure (mmHg)	145 ± 4	139 ± 3	0.227
Diastolic blood pressure (mmHg)	79 ± 2	78 ± 2	0.725
W_{max} (W/kg body wt)	1.9 ± 0.1	1.8 ± 0.2	0.286

Data are means ± SEM unless otherwise indicated. In the non–insulin-treated diabetic patients, glucose, insulin, and oral glucose insulin sensitivity (OGIS) index were determined from an OGTT performed after 2 days of discontinuation of habitual use of oral blood glucose–lowering medication. W, watts; NA, not applicable.

the control and nondaily exercise treatment ($P < 0.05$ for both glucose and insulin) (Fig. 2). Interestingly, also in the nondaily exercise experiment, when a 60-min bout of exercise was performed on the previous day, postbreakfast glucose concentrations were significantly lower compared with the control treatment ($P = 0.022$) (Fig. 2*A*).

24-h glucose concentrations

Average blood glucose concentrations over the 48-h monitoring period were reduced from 9.1 ± 0.4 mmol/L in the control experiment to 8.3 ± 0.3 and 8.3 ± 0.3 mmol/L in the nondaily and daily exercise experiments, respectively ($P < 0.001$ for both exercise treatments) (Fig. 3*A*). No differences were observed in the capacity of both exercise treatments to lower average 48-h glucose concentrations ($P = 1.00$). In addition, a similar effectiveness of both exercise interventions was observed in the first 24 h and second 24 h of the 48-h assessment period (Fig. 3*A*). The blood glucose–lowering effects observed over 48 h did not differ between the insulin- and non–insulin-treated type 2 diabetic patients (exercise × group interaction $P = 0.44$).

Prevalence of hyperglycemia

Despite the continued use of glucose-lowering medication and consumption of a healthy diet, type 2 diabetic patients experienced excessive hyperglycemia (glucose concentrations exceeding 10 mmol/L) throughout a considerable part of the day. In fact, hyperglycemia was experienced for as much as 7:40 ± 1:00 h:min per day (7:27 ± 1:34 and 7:54 ± 1:23 h:min per day in the non–insulin-treated and insulin-treated type 2 diabetic patients, respectively). The prevalence of hyperglycemia was reduced from 7:40 ± 1:00 to 5:46 ± 0:58 and 5:51 ± 0:47 h:min per day when exercise was performed daily or nondaily ($P < 0.001$ for both exercise treatments) (Fig. 3*B*). The effects of exercise on hyperglycemia were comparable between the insulin- and non–insulin-treated subjects (exercise × group interaction $P = 0.43$). When the effects of exercise over both the first and second 24 h of the 48-h assessment period were calculated, daily and nondaily exercise were equally effective in reducing the prevalence of hyperglycemia over both the first and second 24-h periods (Fig. 3*B*).

Prevalence of hypoglycemia

Overall, hypoglycemia was prevalent for an average of 0:46 ± 0:18 h:min over the 48-h monitoring period, representing 2 ± 1% of the total time. The prevalence of hypoglycemia did not change when nondaily or daily exercise was performed during the 48-h period (1:00 ± 0:14 and 0:59 ± 0:14 h:min, respectively; main effect $P = 0.63$). Although we did not observe an exercise × group interaction ($P = 0.54$), the overall prevalence of hypoglycemia was approximately threefold higher in the insulin-treated compared with the non–insulin-treated type 2 diabetic patients (between-group effect $P = 0.012$).

CONCLUSIONS—The current study shows that hyperglycemia is highly prevalent throughout the day in insulin- and non–insulin-treated type 2 diabetic patients. A single bout of merely 30 min of exercise is shown to substantially reduce the prevalence of hyperglycemia throughout the subsequent day. Thirty minutes of daily exercise is as effective as more prolonged 60-min bouts of exercise performed every other day to optimize glycemic control in type 2 diabetic patients.

The current study confirms previous reports (23,24) showing that postprandial hyperglycemia is a largely underestimated problem in type 2 diabetes treatment. Despite the continued use of blood glucose–lowering medication and the provision of a healthy, well-balanced diet, type 2 diabetic patients were shown to experience hyperglycemia for as much as 32 ± 4% of the time (Fig. 3). This finding translates to 7:40 ± 1:00 h:min per day during which blood glucose levels exceeded 10 mmol/L. The prevalence of hyperglycemia was comparable in the insulin-treated and non–insulin-treated type 2 diabetic patients (7:54 ± 1:23 and 7:27 ± 1:34 h:min per day, respectively), suggesting that neither oral blood glucose–lowering medication nor exogenous insulin provides sufficient protection against postprandial hyperglycemia. Given the strong and independent relationship between postprandial blood glucose increments and cardiovascular events (3–5), more effective management of postprandial hyperglycemia is warranted.

In the current study, we show that just 30 min of moderate-intensity exercise substantially reduces the prevalence of hyperglycemia throughout the subsequent day. A single bout of exercise reduced the prevalence of hyperglycemic episodes by nearly 2 h, from 7:40 ± 1:00 to 5:46 ± 0:58 h:min per day (Fig. 3*B*). Moreover, average blood glucose concentrations throughout the subsequent day were reduced by 0.8 mmol/L: from 9.1 to 8.3 mmol/L (Fig. 3*A*). These profound effects of such a short exercise bout seem to be of a magnitude similar to those reported in previous studies following more prolonged bouts of exercise in both insulin-treated (8,9) and non–insulin-treated (7,9) type 2 diabetic patients. Clearly, the prescription of just 30 min of daily exercise represents an effective interventional strategy to

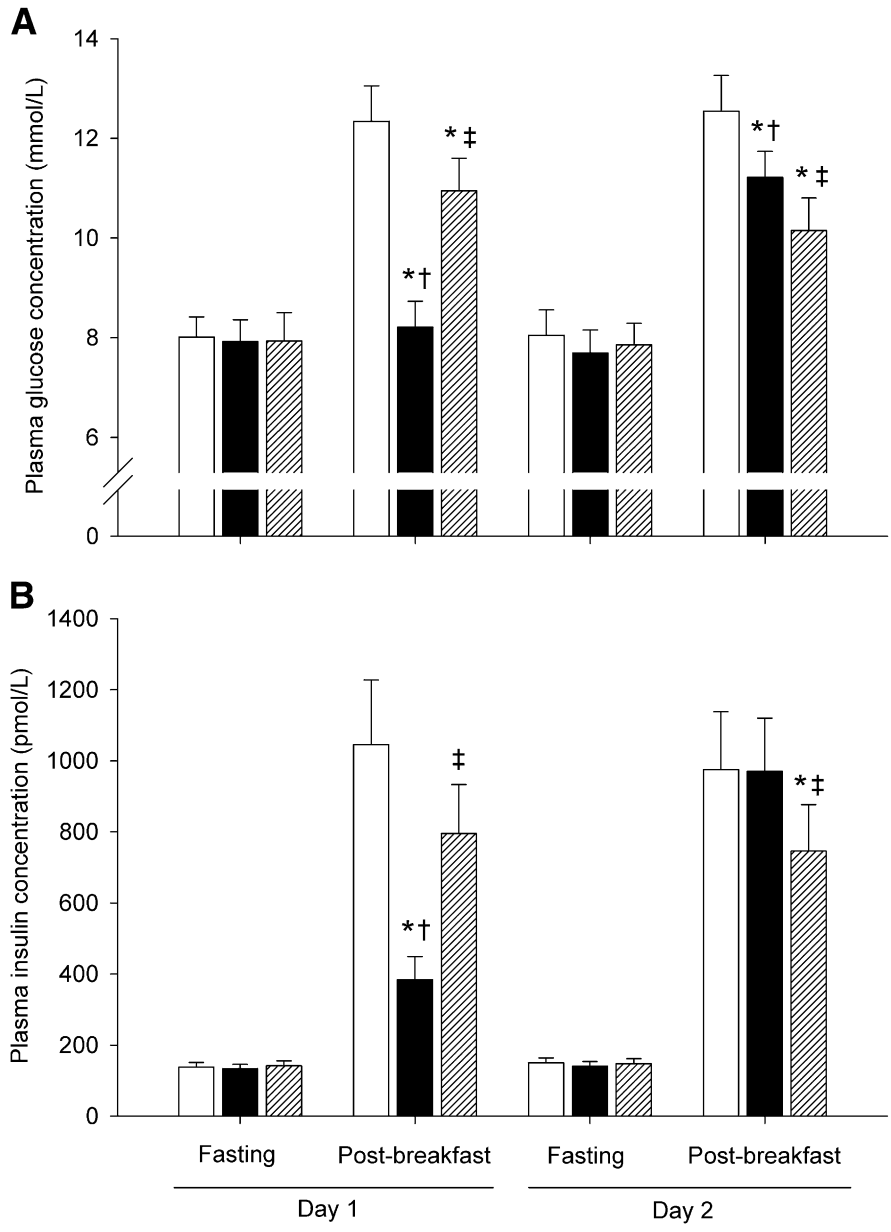

Figure 2—*Average plasma glucose* (A) *and insulin* (B) *concentrations obtained in fasting conditions and 2.5 h following breakfast on days 1 and 2 of an experimental period during which subjects performed no exercise (control [□]) or 60 min of cycling exercise (50% W_{max}) distributed either as a single session per 2 days (nondaily [■]) or as 30 min per day (daily [▨]). Plasma glucose concentrations were determined in all type 2 diabetic patients* (n = *30), whereas plasma insulin concentrations were determined in non–insulin-treated type 2 diabetic patients only* (n = *16). *Significantly different compared with the control trial* ($P < 0.05$). †*Significantly different compared with daily exercise* ($P < 0.05$). ‡*Significantly different compared with nondaily exercise* ($P < 0.05$).

reduce hyperglycemia and improve daily glycemic control in type 2 diabetic patients. As such, the present findings highlight the clinical relevance of exercising at least 30 min per day, which has been advocated by many exercise guidelines as the minimal daily amount of exercise to promote and/or maintain optimal health (15,25,26).

The current study further extends on previous work in this area by investigating the impact of the frequency of exercise on glycemic control throughout the day. A single bout of exercise stimulates blood glucose disposal (27,28) and induces a transient increase in whole-body insulin sensitivity for up to 48 h (29,30). Consequently, it has been speculated that performing exercise on a daily basis may be of even greater benefit with respect to glycemic control compared with exercise bouts performed less frequently (11,16). Therefore, in the current study we compared the impact of 30-min bouts of exercise performed daily with more prolonged 60-min bouts of exercise performed every other day on subsequent glycemic control. The daily bouts of exercise were shown to be equally effective in lowering postprandial hyperglycemia as the more prolonged bouts of exercise performed every other day (Fig. 3). Thus, when total work is being matched, daily exercise of short duration is equally effective as more prolonged bouts of exercise performed less frequently. Consequently, when exercise is not performed every day, patients can compensate by performing more prolonged bouts of exercise every other day.

Both moderate-intensity exercise and high-intensity exercise performed in the postprandial state have been shown to acutely decrease postprandial plasma glucose and insulin concentrations (27,28). In the current study, moderate-intensity exercise was initiated in the early postprandial phase, 90 min after breakfast. Postprandial plasma glucose and insulin concentrations obtained 150 min after breakfast were substantially lower when prior exercise was performed. Interestingly, both plasma glucose and insulin concentrations obtained in this acute postprandial phase were shown to be reduced in a dose-dependent manner after performing 30 or 60 min of exercise (Fig. 2). The attenuated rise in postprandial plasma glucose concentrations following exercise is attributed to a greater glucose uptake and subsequent storage and/or oxidation (10,27). The concomitant reduction in circulating insulin levels clearly reflects the impact of exercise on stimulating insulin-independent glucose disposal. In contrast to the acute phase, a dose-response effect was not observed over the entire 24 h period following exercise. Both the 30- and 60-min exercise bouts were equally effective in improving glycemic control throughout the subsequent day (Fig. 3).

The strong blood glucose–lowering effects induced by exercise may be associated with an augmented risk of developing hypoglycemia in patients with advanced type 2 diabetes (31,32). Particularly, the combined glucose-lowering effects of exercise and exogenous insulin or sulfonylureas may increase the risk for hypoglycemic

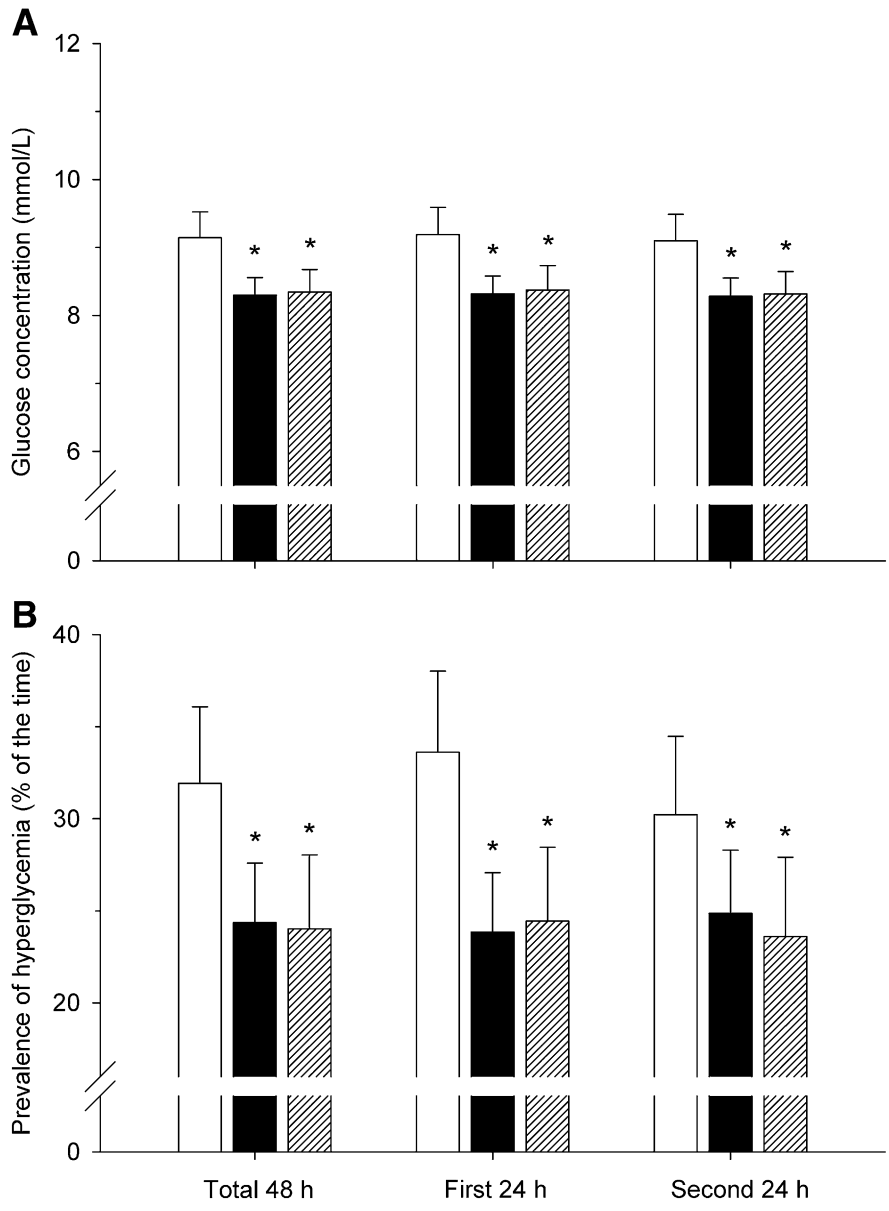

Figure 3—*Average 24-h glucose concentrations* (A) *and the prevalence of hyperglycemia* (B) *in type 2 diabetic patients* (n = *30) determined over the first 24 h, second 24 h, and total 48 h of the assessment period during which subjects performed no exercise (control [□]) or 60 min of cycling exercise (50% W_{max}) distributed either as a single session per 2 days (nondaily [■]) or as 30 min per day (daily [▨]). *Significantly different compared with the control trial* ($P < 0.05$).

episodes. Therefore, we also assessed the prevalence of hypoglycemia in both the insulin- and non–insulin-treated type 2 diabetic patients. Overall, the prevalence of hypoglycemia (here defined as blood glucose concentrations <3.9 mmol/L) was approximately threefold higher in the insulin- compared with the non–insulin-treated type 2 diabetic patients (between-group effect $P = 0.012$). However, exercise did not increase the prevalence of hypoglycemic episodes (main effect $P = 0.63$), and the response to exercise was not different between insulin- and non–insulin-treated type 2 diabetic patients (exercise × group interaction $P = 0.54$). The absence of any exercise-induced hypoglycemia is not surprising, as we ensured that dietary intake was well distributed over the day, with meals and/or snacks ingested prior to and immediately after exercise.

The current study holds several important implications for health care professionals. Frequent short bouts of exercise are equally effective to improve glycemic control as less frequent exercise bouts of a longer duration. Consequently, the total amount of work performed seems to be of prime importance with respect to glycemic control. This view is supported by a recent meta-analysis of Umpierre et al. (17), which demonstrated greater improvements in glycemic control (i.e., HbA_{1c}) following structured exercise training with a total duration of >150 min per week as opposed to <150 min per week. The balance between the frequency and duration of exercise sessions, however, can be used as an instrument to optimize exercise prescription for the individual patient. Depending on the preference of the patient, the presence of comorbidities, and overall training status, more frequent short bouts of exercise can be substituted for less frequent exercise bouts of a longer duration or vice versa. Short bouts of exercise may be particularly useful for patients suffering from reduced exercise tolerance, polyneuropathy, and other diabetic comorbidities, such as micro- and macrovascular complications, which generally reduce the feasibility of performing more prolonged exercise. On the other hand, more prolonged bouts of exercise may offer a time-efficient alternative to daily exercise and might be more feasible for many other diabetic patients who have difficulty scheduling daily exercise in their work routine.

Caution should be taken when translating our findings to the entire population of patients with type 2 diabetes, since patients included in the current study were relatively healthy. Patients suffering from severe long-term complications and reduced exercise tolerance may not be able to perform exercise with the duration and intensity applied in the current study. It should be noted, however, that particularly these patients would benefit from the finding that frequent short bouts are equally effective with respect to glycemic control compared with more prolonged bouts of exercise (11). Nevertheless, the feasibility and effectiveness of an exercise regimen with frequent short bouts of exercise remain to be established in type 2 diabetic patients suffering from long-term complications.

In conclusion, 30 min of exercise substantially reduces the prevalence of hyperglycemia throughout the subsequent day in both insulin- and non–insulin-treated type 2 diabetic patients. Short bouts of exercise performed on a daily basis are equally effective as more prolonged bouts of exercise

performed every other day to improve glycemic control in type 2 diabetic patients.

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J.-W.v.D. designed the study, collected and researched data, and wrote the manuscript. K.T. collected and researched data and contributed to the discussion. C.D.A.S. and F.H. contributed to the discussion and reviewed and revised the manuscript. L.J.C.v.L. designed the study, researched data, and wrote the manuscript. J.-W.v.D. and L.J.C.v.L. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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