



Aalborg Universitet

AALBORG UNIVERSITY
DENMARK

A self-monitoring approach for evaluating the effect of 3 weeks of high-intensity training in patients with type 2 diabetes mellitus

An intervention study

Dissing, Anne-Mette Lücke; Johansen, Mette Dencker; Pilegaard, Morten; Hejlesen, Ole Kristian

Published in:
Obesity Medicine

DOI (link to publication from Publisher):
[10.1016/j.obmed.2019.01.001](https://doi.org/10.1016/j.obmed.2019.01.001)

Creative Commons License
CC BY-NC-ND 4.0

Publication date:
2019

Document Version
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Dissing, A-M. L., Johansen, M. D., Pilegaard, M., & Hejlesen, O. K. (2019). A self-monitoring approach for evaluating the effect of 3 weeks of high-intensity training in patients with type 2 diabetes mellitus: An intervention study. *Obesity Medicine*, 13, 45-51. <https://doi.org/10.1016/j.obmed.2019.01.001>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- ? Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- ? You may not further distribute the material or use it for any profit-making activity or commercial gain
- ? You may freely distribute the URL identifying the publication in the public portal ?

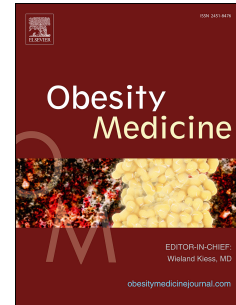
Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Accepted Manuscript

A self-monitoring approach for evaluating the effect of 3 weeks of high-intensity training in patients with type 2 diabetes mellitus. An intervention study

Anne-Mette Dissing, Mette D. Johansen, Morten Pilegaard, Ole Hejlesen



PII: S2451-8476(18)30069-1

DOI: <https://doi.org/10.1016/j.obmed.2019.01.001>

Reference: OBMED 77

To appear in: *Obesity Medicine*

Received Date: 4 October 2018

Revised Date: 17 December 2018

Accepted Date: 5 January 2019

Please cite this article as: Dissing, A.-M., Johansen, M.D., Pilegaard, M., Hejlesen, O., A self-monitoring approach for evaluating the effect of 3 weeks of high-intensity training in patients with type 2 diabetes mellitus. An intervention study, *Obesity Medicine* (2019), doi: <https://doi.org/10.1016/j.obmed.2019.01.001>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

indA self-monitoring approach for evaluating the effect of 3 weeks of high-intensity training in patients with type 2 diabetes mellitus. An intervention study.

Anne-Mette Dissing^{a,b}, Mette D. Johansen^b, Morten Pilegaard^c, Ole Hejlesen^b

^a Department of Physiotherapy, University College of Northern Jutland, Denmark

^b Department of Health Science and Technology, Aalborg University, Denmark

^c Department for English, Aarhus University, Denmark

Corresponding author:

Anne-Mette Dissing

Department of Physiotherapy, UCN

Selma Lagerloefs Vej 2

DK-9220 Aalborg

Denmark

E-mail: atd@ucn.dk

Declarations of interest: none.

1 Introduction

The global incidence of diabetes is growing. It is estimated that the incidences will rise from 425 million in 2017 to 629 million in 2045 [1], with type 2 diabetes mellitus (T2DM) accounting for 90% [2]. Furthermore, recent years have seen a lower average age of diabetes onset [3] so that more individuals may be expected to live longer with their disease and to face an increased accumulated lifetime risk of complications.

Physical exercise is one of three cornerstones in the treatment in patients with T2DM as it slows disease progression and delays development of complications [4–7]. Regular strength and endurance training has beneficial effects on factors related to T2DM [8,9], but physical exercise must be performed regularly to be effective. The American Diabetes Association therefore recommends a weekly minimum duration of 150 minutes of moderate to vigorous exercise [10].

Recent research shows that the intensity of training matters, too; and high-intensity training (HIT) has been shown to be beneficial in patients with T2DM; viz. HIT positively affects blood glucose by reducing 24 h blood glucose concentration [11], decreasing fasting and 2h glucose and decreasing HbA_{1c} [12]. This positive effect may be attributable to several factors such as increased GLUT4 content, increased activity of citrate synthase and increased protein content in the electron transport chain [11]. Endothelial physiology has also been improved, as well as endothelial-dependent vasodilator response and functional capability [13]. Research also suggests that HIT may outperform other kinds of training because it addresses a main concern voiced by patients with T2DM, namely that lacking time is claimed to be a barrier to regular training [14,15].

Monitoring the effect of training, most prior research has deployed invasive technologies such as tissue biopsies, blood tests and ultrasound [11,16–19]. These technologies command expert knowledge and special equipment, which is usually available only at hospitals or dedicated facilities.

Remarkably little effort has gone into exploring how health improvements may be monitored using simpler techniques that may be mastered by the patients themselves, even in their own homes. This is surprising as the introduction of simple techniques that may be used by the patients themselves in their own homes may support patient motivation and self-efficacy regarding training.

A battery of simple methods for monitoring the effect of HIT training could include taking the oral glucose tolerance test (OGTT), measuring blood pressure, monitoring weight and calculating fat composition.

No current research, however, has investigated if the effect of short-term HIT can be measured using simple methods. If this shows to be the case, it opens for the opportunity for the patients to measure the effect of training by themselves at home. Likewise, extant knowledge on the ability of patients with diabetes to comply with HIT is sparse.

The dual aim of the present study is, first, to investigate to which extent the effect of a short period of HIT leads to measurable changes detectable with simple self-testing methods in patients with T2DM; second, to investigate these patients' compliance with HIT.

2 Methods

2.1 Participants

Ten adults with T2DM recruited from the healthcare centre in Aalborg Municipality (Sundhedscenter Nordkraft), Denmark, were recruited in collaboration with the physiotherapist employed at the healthcare centre. The participants were asked to obtain oral approval from their general practitioner (GP) of their participation in HIT to ensure that this was not contraindicated. Further criteria for inclusion were manifest T2DM diagnosed by GP and being able to participate in training performing the fixed test on set training days. Exclusion criteria were use of pacemaker and any conditions contraindicating training at high intensity.

2.2 Experimental design

2.2.1 Study overview

$VO_{2\max}$ tests were performed on day -2, at baseline (day 0) and after 21 days, and training was performed on set days (day 3, 5, 7, 10, 12, 14, 17 and 19) as shown in Table 1. Baseline measures and post-tests were performed at day 0 and 21, respectively.

Table 1: Study overview

Day	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Activity	$VO_{2\max}$		Base line			T		T		T			T		T		T			T		T		Post-test

T: training

At day -2, a $VO_{2\max}$ test was performed in order for the patient to become familiar with the test before the first actual test at day 0. The pre-test at day 0 was carried out at least two days before the first training session in order to allow patients to recover after the $VO_{2\max}$ test before training. After 8 times of training, the post-test was undertaken at day 21, i.e. two days after the last training session in order to avoid any acute effect of training. Both baseline and post-test were carried out on Fridays and training days were Mondays, Wednesdays and Fridays. The training was scheduled on the time of the day most suitable for the patients to limit time-related barriers to participate in training. This was primarily in the mornings or early afternoon.

The pre- and post-tests contained the following: OGTT, blood pressure measurement, weight and fat% measurements and $VO_{2\max}$ test. Pretesting also contained a questionnaire about the patients' daily level of physical activity and their medical history.

2.2.2 Oral Glucose Tolerance Test (OGTT)

Participants were instructed to continue a normal diet in the days leading up to the test. At the day of testing, they should meet fasting (and have fasted for at least 10 hours); and they were asked to take no medications that could influence blood glucose levels in the fasting hours (two forgot and they were instructed also to take medications prior to the post-test). At baseline, a small blood sample was collected by finger prick to determine fasting capillary blood glucose level (Accu-Check® Aviva, Basel, Switzerland). The fingertip was disinfected before the finger prick and the first drop of blood was removed before applying a drop of blood in the glucose meter. The participants were then instructed to drink 75 mg of glucose (82.5g glucose monohydrate) dissolved into 300 ml of water. Blood samples were collected after 30, 60, 90 and 120 minutes using finger prick.

2.2.3 Blood pressure

Blood pressure was measured after 10 min of rest in a sitting position. An automatic blood pressure monitor was used (Omron, M4-I), and three measures were made. The lowest of the three values was used for calculations.

2.2.4 Weight and fat%

Weight and fat% were measured on a Tanita® digital scale with bioelectrical impedance (Tanita MC-180MA, Tokyo, Japan). The participants were instructed to step on the scale barefooted and to keep the hands with the handgrips slightly elevated from the torso.

2.2.5 VO_{2max}

Bicycle test was performed on a bike ergometer (Corival Lode, Gronningen, The Netherlands) to exhaustion with direct measurement of oxygen consumption by breath-by-breath on Jaeger Masterscreen CPX (Intramedic A/S, Lyngby, Denmark). The participants were informed about the test-protocol before applying the equipment used for the test. Then there was a 5-min warm-up period on 50-75 watt followed by incremental 25 watt intensity increases per minute until exhaustion. The test was considered a VO_{2max} if the respiratory exchange ratio (RER) value exceeded 1.10. Otherwise, it was categorised as a VO_{2peak} test.

2.2.6 Physical activity

Physical activity was assessed by using the Physical Activity Scale (PAS) questionnaire [20]. PAS1 was used instead of the PAS2 as not all the participants were working in the daytime. The participants were asked to report time spent on different activities on an average weekday before the intervention. These activities is categorised into nine different categories with a corresponding metabolic equivalent (1 MET \sim 1 kcal/kg/h) ranging from low to high intensity. A total metabolic equivalent of task (MET) score was calculated as time spent on each category multiplied by the corresponding MET, and then all nine categories were added together. The categories were sleep (0.9 MET), TV-viewing/reading (1.0 MET), sitting/working (1.5 METs), standing up (2.0 METs), light work (3.0 METs), light-to-moderate activity (4.0 METs) moderate activity (5.0 METs), moderate-to-high activity (6.0 METs) and high-intensity activity (>6 METs). As for the high intensity, a level of 7 METs was chosen in this study.

2.2.7 Training

The training consisted of 10 x 60 sec work on an indoor exercise bike at an intensity of \sim 90% of max heart rate (HR_{max}) interspersed by 60 sec of recovery. This training protocol was applied 3 times per week (Mon-Wed-Fri) with a total amount of eight training sessions. Little et al (2011) have previously described this protocol [11]. The HR used for training was calculated based on the max HR found by the VO_{2max} test at baseline and measured by a Polar H7 Smart Bluetooth (Polar, Holte, Denmark). The intensity of 90% of HR_{max} was achieved by adjusting the resistance and/or pedal cadence (the last in the range of 80-110 rpm). During the recovery phase, the participants pedalled slowly at a lower intensity (\sim 50 watt). Each interval was scored on Borg RPE Scale (rate of perceived exertion, RPE), which is a subjective scale where the participants' experience of exhaustion is expressed in a number from 6 to 20. The value 6 is categorised as resting and 20 is exhaustion [21]. Perceived enjoyment of HIT was assessed using a 9-point Likert scale ranging from 1 (not enjoyable at all) to 9 (very enjoyable). After each training session, the participants were asked how enjoyable they would think it would be to engage in 1) a single bout of HIT (10 x 1 min) and 2) HIT at least 3 times/wk for the next 4 wk, and they were asked to rank their answers on the 9-point Likert scale. After each training session, the patients were encouraged to be seated and recover for a while to ensure well-being after training and observe for symptoms related to hypo- and hyperglycaemia.

2.3 Statistical analysis

All analyses were performed using IBM SPSS Statistics software (version 23), and data are presented as means \pm standard deviation (SD) unless otherwise stated. Changes in baseline and post-test values were assessed using the non-parametric alternative to the parametric Student's t-test (Wilcoxon signed-rank test) as the sample size was too low to assume normality. P values <0.05 were considered statistically significant

The measured HR was converted to intensity as percentage of max HR by the following formula: $(\text{measuredHR}/\text{maxHR}) \times 100$. The subjective given value on Borg REP scale was converted to intensity by the following formula: $(\text{given value}/\text{max value}) \times 100$.

The participants signed informed consent after receiving written and oral information. The study was presented to the local Ethics Committee but needed no ethical approval. The study was registered with Clinicaltrials.gov.

3 Results

3.1 Patients characteristics and physical values

Ten patients (nine men and one woman) with T2D participated in the study. The average age was 56.1 ± 12.6 years and the diabetes age was 2.7 ± 1.9 years. Based on the PAS, the average MET time for the patients was 51.55 ± 14.11 kcal $\text{kg}^{-1} \text{h}^{-1}$. The patients' physical values at baseline and after eight times of HIT are shown in Table 2.

Three patients reported slightly reduced sensitivity in their feet as a complication of the T2DM. Of the ten patients included, only one patient took no medications. The remaining nine patients were on oral antidiabetics (of which two were supplemented with multiple daily injections of insulin analogues). Furthermore, medications were given for the following comorbidities: elevated cholesterol (six patients), hypertension (five patients), atherosclerosis (one patient), hypokalaemia (one patient), reduced metabolism (one patient), diuresis (one patient) and arrhythmia (one patient). No patients reported regular monitoring of their blood glucose.

Table 2: Physical values at baseline and after eight times of HIT.

	Baseline	Post-test	p-values (Wilcoxon)
Weight (kg)	108.3 \pm 14.7	107.5 \pm 14.6	0.047
Total fat (%)	31.83 \pm 5.8	31.57 \pm 5.6	0.173
Fasting capillary blood glucose (mmol/l)	7.33 \pm 1.97	6.97 \pm 1.5	0.185
2h capillary blood glucose (mmol/l)	10.9 \pm 3.5	9.89 \pm 3.2	0.047
VO _{2 max} (l min ⁻¹)	2.75 \pm 0.67	2.76 \pm 0.78	0.959
VO _{2 max} (ml kg ⁻¹ min ⁻¹)	25.4 \pm 4.3	25.5 \pm 5.4	0.919
Systolic blood pressure (mmHg)	145 \pm 16	136 \pm 18	0.053
Diastolic blood pressure (mmHg)	90 \pm 10.9	85 \pm 10	0.015

Values are in mean \pm standard deviation (SD)

3.2 Physical activity

Physical activity measured as mean MET time on an average weekday was 51.55 ± 14.11 kcal/kg/day (range 35.02 – 82).

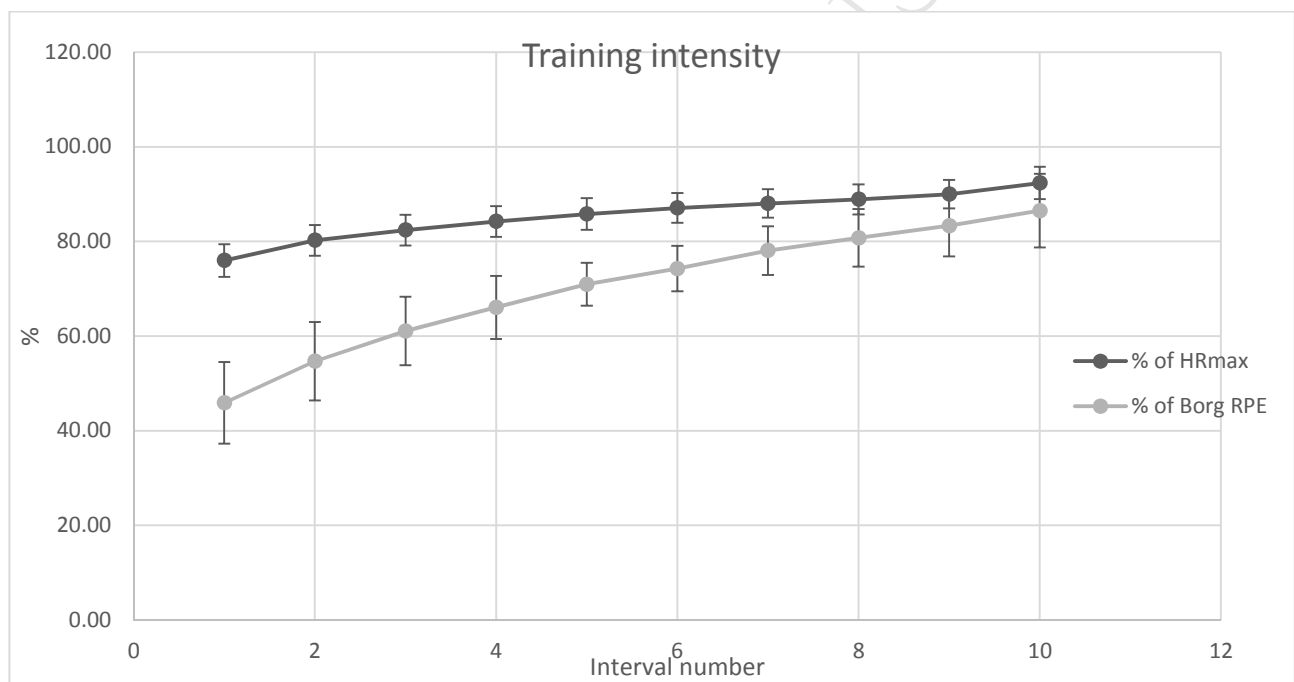
3.3 Compliance and perceived enjoyment

All the ten recruited patients with T2DM showed 100% compliance on all study parameters. HIT training was well tolerated, viz. 6.10 ± 1.23 for the question “How enjoyable would it be to engage in a single bout of HIT (10 x 1 min)” and 6.5 ± 1.17 for the other question “How enjoyable would it be to engage in HIT at least three times/wk for the next 4 wk”.

3.4 Intensity

Figure 1 shows the intensity of training measured by HR as percentage of max HR and the intensity calculated by the Borg RPE scale. The average intensity was $85.49 \pm 4.92\%$ of HR_{max} for all participants at all intervals. The calculated intensity using RPE was $70.15 \pm 13.17\%$.

Figure 1: The mean intensity for each interval measured in percentage of HR_{max} and percentage of Borg RPE scale.



3.5 Glycaemic control

Glycaemic control measured by fasting blood glucose and 2h blood glucose at baseline and after eight times of HIT are shown in Figure 2.

Eight times of HIT showed no effect on fasting blood glucose (7.33 ± 1.97 mmol/l to 6.97 ± 1.5 mmol/l, $p=0.185$; Figure 1). Blood glucose measured 2 hours after the glucose load in OGTT showed a significant decrease in blood glucose values (10.9 ± 3.5 mmol/l to 9.89 ± 3.2 mmol/l $p=0.047$; Figure 2).

Figure 2: Glycemic control measured as fasting blood glucose concentration and 2h blood glucose concentration. Measured at baseline and after eight times of training.

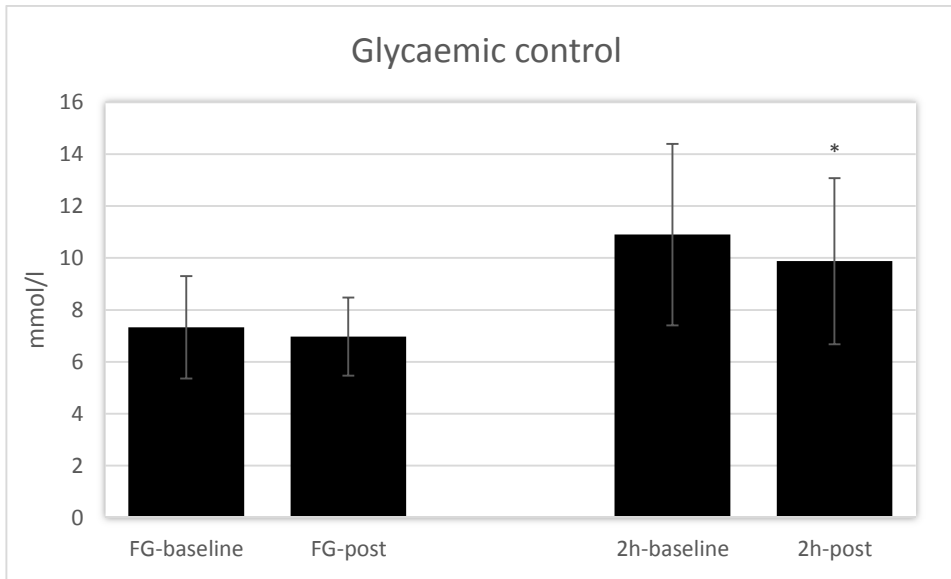


Figure 2: 2 hour blood glucose baseline 10.9 ± 3.5 mmol/l and posttest 9.89 ± 3.2 mmol/l. $P = 0.047$. Fasting blood glucose baseline 7.33 ± 1.97 mmol/l and post-test 6.97 ± 1.5 mmol/l. $P=0.185$

3.6 Blood pressure

Figure 3 displays the diastolic and systolic blood pressure measured at baseline and after eight times of HIT. It can be seen in the figure that HIT caused a reduction in diastolic blood pressure (90 ± 10.9 mmHg to 85 ± 10 mmHg. $p=0.015$), whereas no change was observed in the systolic pressure (145 ± 16 mmHg to 136 ± 18 mmHg. $p=0.053$) (Figure 3)

Figure 3: Blood pressure measured at baseline and after 8 times of HIT

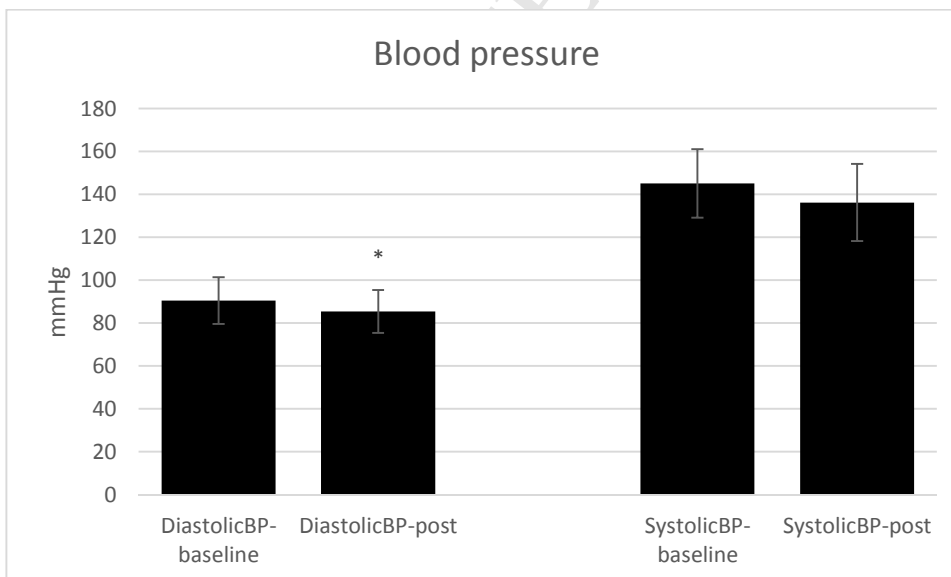


Figure 3: Diastolic blood pressure baseline 90 ± 10.9 mmHg and post-test 85 ± 10 mmHg. $P=0.015$. Systolic blood pressure baseline 145 ± 16 mmHg and post-test 136 ± 18 mmHg. $P=0.053$

3.7 Body composition

Post-test revealed a significant decrease in weight from 108.3 ± 14.7 kg to 107.5 ± 14.6 kg ($p=0.047$) after eight times of HIT. Total fat percent showed no change ($31.83 \pm 5.8\%$ to 31.57 ± 5.6 . $p= 0.173$) (Table 2).

4 Discussion

This is to our knowledge the first study reporting the effect of HIT using simple, non-invasive methods that have the potential to be applied in the daily life of patients with T2DM by the patients themselves.

The aims of the study were to investigate to which extent a short period of HIT can improve cardio-metabolic status in patients with T2DM using simple self-testing methods, and to investigate these patients' compliance with HIT.

We observed significant improvements in key parameters such as 2h-glucose, weight and diastolic blood pressure after only eight times of HIT. We also observed a high HIT training compliance.

4.1 Physical activity

Using PAS, the participants scored 51.55 ± 14.11 kcal/kg/day which is a more than adequate physical activity level and well above the general suggested threshold of 45 kcal/kg/day that corresponds to a moderate physical activity level [22]. However, the PAS level was based on a self-reporting questionnaire; and it is likely that these self-reported measures were overestimated as the cardiorespiratory fitness measures showed only low-to-very-low scores related to age according to the chart of Astrand [23]. This presumption is further supported by Thomas et al (2004), who showed that 67% of a sample size of 406 patients with T2DM was categorised as inactive [24]. Therefore, either we have recruited very active participants, or they have overestimated the level of their physical activity in the questionnaire; we believe that the latter explanation is the more likely one in light of their $VO_{2 \max}$ values.

4.2 Exercise capacity

In the present study, HIT intensity was scored lower by the RPE as shown in Figure 1, which is a subjective measure, than by HR, which is an objective measure. These findings are in agreement with earlier studies reporting an increased risk of exercising at higher intensity when using RPE in patients with T2DM [25] and a low validity by using RPE in indoor cycling [26]. This discrepancy between RPE and HR measures was particularly outspoken in the first intervals. Altogether, this indicates that HR is more valid than RPE for measuring intensity and preventing exercising at a too high intensity.

4.3 Glycaemic control

We found a marked difference between the degree of glycaemic control assessed by fasting blood glucose (Figure 2) which remained constant (baseline: 7.33 ± 1.97 mmol/l; post-test: 6.97 ± 1.5 mmol) and 2h OGTT (baseline: 10.9 ± 3.5 mmol/l; post-test: 9.89 ± 3.2) which decreased significantly ($P = 0.047$). Previous studies report divergent results of HIT on fasting blood glucose [12,16–19]. These discrepancies could be rooted in the general limitation associated with using fasting blood glucose as a measure of glycaemic control, viz. that the fasting blood glucose level depends on the food ingested one or more days before the level is measured [27].

One possible solution to this challenge could be to control food intake on the day or the days leading up to test days, but this approach does not resemble everyday life and cannot be easily integrated into daily routines, wherefore we deselected this option.

We chose to use the OGTT, because it is less prone to reflect the impact of previous food intake than fasting blood glucose. Although OGTT outperforms fasting blood glucose in terms of reliability, only few studies have used the OGTT to evaluate the effect of HIT, and their results are conflicting. One study found a significant decrease in 2h glucose [12] after 8 weeks of using the same protocol as in the present study. Another study reports no effect after 12 weeks using a different training protocol [16]. OGTT simply depicts the change in blood glucose after a glucose challenge and does not explain the physiological and pathophysiological mechanisms behind. It is therefore often supplemented with other tests with more explanatory power, e.g. the HOMA-index [12,16,18] and biopsy [28]. However, in the present study, we wished to examine the effect of HIT using relatively simple methods and not to explore the mechanisms behind the effect, wherefore these other tests were deselected.

We also deselected other methods like HbA_{1c}, which is often used to measure long-term control of blood glucose, or continuous glucose monitoring (CGM) as used by Little et al (2011) [11]. We chose not to use HbA_{1c}, which reflects the average glucose concentration over the past 8 to 12 weeks [29], because the training period in the present study was only 2.5 weeks and we therefore could not expect to find an effect on HbA_{1c}. Furthermore, measuring the HbA_{1c} is not doable at home by the patients themselves because laboratory equipment is needed. Retrospectively, a baseline HbA_{1c} would have been appropriate to describe the patient's diabetes-status at baseline; however, this was not included as the aim of the study was to examine the effect of HIT by using simple methods. We considered using CGM, which might have shown improvements in the present study as was the case in the study of Little et al (2011) [11], who used the same training protocol and almost the same duration. However, CGM requires training and considerable knowledge making this method more complicated than OGTT, which can be carried out by the patients themselves at home with the use of a glucose solution and blood from a finger prick. In addition, the result from OGTT can easily be interpreted.

4.4 Blood pressure

In the present study, the diastolic blood pressure was decreased significantly (baseline: 90±10.9 mmHg; post-test: 85±10 mmHg. P=0.015), whereas the systolic pressure showed no change (baseline: 145±16 mmHg; post-test: 136±18 mmHg). Other studies show diverging results concerning changes in blood pressure. One study found a decrease in both pressures, possibly due to a longer training period [12]; another showed no lowering effect on blood pressure after 12 weeks of HIT [16] even though the baseline values were almost similar in the two studies, and in both cases close to normal. Alvarez et al (2016) found only a decrease in systolic blood pressure after 16 weeks of training [19], whereas in the present study, a significant decrease was found in diastolic pressure. An explanation for this disparity between the results of our study and those of others could be a higher starting value in the diastolic pressure in the present study (90 ± 10,9 mmHg) than in the study by Alvarez et al (2016) (77 ± 1 mmHg) [19]. Altogether, the results of the impact of HIT on blood pressure show inconsistency, and further studies are recommended to clarify this issue.

4.5 Body composition

In the present study, we detected no change in fat%, but a significant decrease in weight (baseline: 108.3±14.7 kg; post-test: 107.5±14.6 kg. P=0.047). Other studies report variable effects of training on fat percentage and weight. Some show a positive effect on both weight and fat% [12,17], whereas others show an effect only on fat% [16] or weight [19]; and others again found no loss of either fat or weight [11,18]. The diversity in findings could be attributed to the diversity in methods applied. The present study specifically deploys simple methods, which, of course, all things equal will be less reliable than the DXA,

which is estimated to be a very valid measure (Prior, 1997). Still the present study used bioelectric impedance because of its feasibility. Furthermore, it was not expected to measure a change in fat% in the present study due to the short training period.

4.6 Compliance

In the present study, training compliance reached 100%. This high level of compliance largely corresponds with levels reported by other studies which used different HIT protocols and different durations of training period (2 weeks to 12 weeks) [11,12,16,18,30,31]. Altogether, this implies a high feasibility of HIT.

The present study scored lower than the study of Little et al. on the fondness of HIT (6.10 ± 1.23 vs. 8.1 ± 1.0 and 6.5 ± 1.17 vs. 7.9 ± 1.0 in the two questions, respectively), but together the results indicate a fairly good response towards HIT.

4.7 Limitations

A measure of caution is required when interpreting the results of the present study. The sample size is too small to make conclusions generalizable to the entire population of patients with T2DM, and more studies with larger sample sizes are therefore needed to establish the effect. Furthermore, the duration of the training period was very short (only eight times of training); even so, we found that HIT did have a beneficial effect. This suggests that the effect of HIT can be ascertained very quickly, even when measured by simple methods. Though, it should also be taken into consideration that the included patients' fasting and 2h glucose concentrations indicated a relatively good glycaemic control already at baseline.

We also speculate that patients may find it easier to commit themselves to a short 2.5-week HIT training schedule without losing enthusiasm, and that compliance would decline if the HIT training schedule was considerably longer.

The methods for monitoring HIT training progress in this study were chosen with a view to their potential use in the patients' daily lives. We therefore deliberately deselected golden standard methods otherwise used to measure the effect of training on blood glucose control, e.g. biopsies, venous blood samples, clamps, etc.

In patients with diabetes (both type 1 and 2) taking insulin, hypoglycaemia is a risk factor during and after training [32]. Performing intense training as HIT can cause post-training hyperglycaemia in patients with type 1 diabetes [33]. In the present study, no blood glucose was measured after training and neither a hypo- nor a hyperglycaemic status could therefore be detected in the two patients using insulin analogues. Though, no symptoms were detected in the recovery state immediate after training or reported from the patients between training sessions regarding this issue. Still, this aspect should be taken into considerations in future studies

4.8 Perspectives

We found that patients themselves may monitor HIT progress; and we speculate that this will increase their overall compliance with training. However, the practicality of self-monitoring relies on the patient's ability to use the simple methods and to interpret the results. Using this approach should therefore include thorough education both in the use of these methods, the frequency of measuring and how to understand the results. This should be addressed in future studies. Further studies into the link between patient empowerment and how own responsibility reflects on training compliance are warranted. Further studies are also needed to study the usability of OGGT as a method performed by the patients themselves.

5 Conclusion

In conclusion, this study shows beneficial improvements in factors relating to T2DM after performing HIT only eight times. These improvements were shown by the use of simple methods that are easily transferred into daily life, giving patients with T2DM the opportunity to monitor effects to HIT and thereby increase their compliance to training. Further studies are needed to examine if the effect from this study can be replicated in a larger scale. Also, there are diverging results from different studies concerning fat% and blood pressure, among others, and the effect of HIT on these factors needs to be studied further.

Acknowledgements

The authors thank the Sundhedscenter Nordkraft for their collaboration. The authors especially thanks Physiotherapist Anders Binett Eriksen and Physiotherapist Jytte Olsen for establishing the initial contact with patients with type 2 diabetes Mellitus.

Funding

This work was funded by the Department of Physiotherapy, University College of Northern Jutland, Denmark, "*Technologies closely connected to Citizens` Health*", University College of Northern Jutland, Denmark and Department of Health Science and Technology, Aalborg University, Denmark. The funders were not involved in study design.

References

- [1] International Diabetes Federation. Diabetes Atlas 8th Edition, <http://www.diabetesatlas.org/>; 2017 [accessed 5 September 2018].
- [2] International Diabetes Federation. Types of Diabetes, <https://www.idf.org/aboutdiabetes/what-is-diabetes/types-of-diabetes.html>; 2017 [accessed 5 September 2018].
- [3] Al-Saeed AT, Constantino MI, Molyneaux L, D'Souza M, Limacher-Gisler F, Luo C, Wu T, Twigg SM, Yue DK, Wong J. An inverse relationship between age of type 2 diabetes onset and complication risk and mortality: The impact of youth-onset type 2 diabetes. *Diabetes Care* 2016;39(5):823-829. doi:10.2337/dc15-0991
- [4] Pedersen BK, Saltin B. Exercise as medicine - Evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sport* 2015;25:1–72. doi:10.1111/sms.12581.
- [5] Sanz C, Gautier J-F, Hanaire H. Physical exercise for the prevention and treatment of type 2 diabetes. *Diabetes Metab* 2010;36:346–51. doi:10.1016/j.diabet.2010.06.001.
- [6] Hopps E, Canino B, Caimi G. Effects of exercise on inflammation markers in type 2 diabetic subjects. *Acta Diabetol* 2011;48:183–9. doi:10.1007/s00592-011-0278-9.
- [7] Colberg SR, Sigal RJ, Fernhall B, Regensteiner JG, Blissmer BJ, Rubin RR, et al. Exercise and type 2 diabetes: The American College of Sports Medicine and the American Diabetes Association: Joint position statement. *Diabetes Care* 2010;33. doi:10.2337/dc10-9990.
- [8] Van Dijk JW, Manders RJF, Tummers K, Bonomi a. G, Stehouwer CD a, Hartgens F, et al. Both resistance- and endurance-type exercise reduce the prevalence of hyperglycaemia in individuals with impaired glucose tolerance and in insulin-treated and non-insulin-treated type 2 diabetic patients. *Diabetologia* 2012;55:1273–82. doi:10.1007/s00125-011-2380-5.
- [9] Thomas D, Elliot EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database of Systematic Review* 2006, Issue 3. doi:10.1002/14651858.CD002968.pub2.www.cochranelibrary.com.
- [10] American Diabetes Association. Standards of Medical Care in Diabetes. *Clin Diabetes* 2017;35(1):5-26. doi:10.2337/cd16-0067.
- [11] Little JP, Gillen JB, Percival ME, Safdar A, Tarnopolsky M a, Punthakee Z, et al. Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. *J Appl Physiol* 2011;111:1554–60. doi:10.1152/jappphysiol.00921.2011.
- [12] Madsen SM, Thorup AC, Overgaard K, Jeppesen PB. High Intensity Interval Training Improves Glycaemic Control and Pancreatic β Cell Function of Type 2 Diabetes Patients. *PLoS One* 2015;10:e0133286. doi:10.1371/journal.pone.0133286.
- [13] da Silva CA, Ribeiro JP, Canto JC a U, da Silva RE, Silva Junior GB, Botura E, et al. High-intensity aerobic training improves endothelium-dependent vasodilation in patients with metabolic syndrome and type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2012;95:237–45. doi:10.1016/j.diabres.2011.09.034.
- [14] Trost SG, Owen N, Bauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. *Med Sci Sports Exerc* 2002;34:1996–2001. doi:10.1249/01.MSS.0000038974.76900.92.
- [15] Korhakangas EE, Alahuhta MA, Laitinen JH. Barriers to regular exercise among adults at high risk or

- diagnosed with type 2 diabetes: A systematic review. *Health Promot Int* 2009;24:416–27. doi:10.1093/heapro/dap031.
- [16] Cassidy S, Thoma C, Hallsworth K, Parikh J, Hollingsworth KG, Taylor R, et al. High intensity intermittent exercise improves cardiac structure and function and reduces liver fat in patients with type 2 diabetes: a randomised controlled trial. *Diabetologia* 2016;59:56–66. doi:10.1007/s00125-015-3741-2.
- [17] Lee SS, Yoo HJ, Yong SS. Effect of the low- versus high-intensity exercise training on endoplasmic reticulum stress and GLP-1 in adolescents with type 2 diabetes mellitus. *J Phys Ther Sci* 2015;27:3063–3068. doi:10.1589/jpts.27.3063.
- [18] Shaban N, Kenno KA, Milne KJ. The effects of a 2 week modified high intensity interval training program on the homeostatic model of insulin resistance (HOMA-IR) in adults with type 2 diabetes. *J Sports Med Phys Fitness* 2014;54:203–9.
- [19] Alvarez C, Ramirez-Campillo R, Martinez-Salaza C, Mancilla R, Flores-Opazo M, Cano-Montoya J, Ciolac EG. Low-Volume High-Intensity Interval Training as a Therapy for Type 2 Diabetes. *Int J Sports Med* 2016;37(9):723–9. doi:10.1055/s-0042-104935.
- [20] Aadahl M, Jørgensen T. Validation of a new self-report instrument for measuring physical activity. *Med Sci Sports Exerc* 2003;35:1196–202. doi:10.1249/01.MSS.0000074446.02192.14.
- [21] Borg G, Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med* 1970;2:92–8.
- [22] Aadahl M, Kjær M, Jørgensen T. Associations between overall physical activity level and cardiovascular risk factors in an adult population. *Eur J Epidemiol* 2007;22:369–78. doi:10.1007/s10654-006-9100-3.
- [23] ASTRAND I, ASTRAND I. Aerobic work capacity in men and women with special reference to age. *Acta Physiol Scand Suppl* 1960;49:1–92.
- [24] Thomas N. Barriers to physical activity in patients with diabetes. *Postgrad Med J* 2004;80:287–91. doi:10.1136/pgmj.2003.010553.
- [25] Unick JL, Gaussoin S, Bahnson J, Crow R, Curtis J, Killean T, et al. Validity of rating perceived exertion in patients with type 2 diabetes. *J Nov Physiother Phys Rehab* 2014;1(1):4–12. doi: 10.17352/2455-5487.000002.
- [26] Muyor JM. Exercise Intensity and Validity of the Ratings of Perceived Exertion (Borg and OMNI Scales) in an Indoor Cycling Session. *J Hum Kinet* 2013;39:93–101. doi:10.2478/hukin-2013-0072.
- [27] Drivsholm T, Hansen C, Kristensen JK, Lassen B, Schultz-Larsen P HD. Type 2-diabetes - et metabolisk syndrom. *Klin Vejil Almen Praksis* 2012:Appendix 1. http://vejledning.dsam.dk/media/files/1/diabetes_bilag1.pdf [accessed 5 September, 2018].
- [28] Segerström ÅB, Elgzyri T, Eriksson K-F, Groop L, Thorsson O, Wollmer P. Exercise capacity in relation to body fat distribution and muscle fibre distribution in elderly male subjects with impaired glucose tolerance, type 2 diabetes and matched controls. *Diabetes Res Clin Pract* 2011;94:57–63. doi:10.1016/j.diabres.2011.05.022.
- [29] Nathan DM, Turgeon H, Regan S. Relationship between glycated haemoglobin levels and mean glucose levels over time. *Diabetologia* 2007;50:2239–44. doi:10.1007/s00125-007-0803-0.
- [30] Maillard F, Rousset S, Pereira B, Traore A, de Pradel Del Amaze P, Boirie Y, et al. High-intensity

interval training reduces abdominal fat mass in postmenopausal women with type 2 diabetes. *Diabetes Metab* 2016;42:433–41. doi:10.1016/j.diabet.2016.07.031.

- [31] Terada T, Friesen A, Chahal BS, Bell GJ, McCargar LJ, Boulé NG. Feasibility and preliminary efficacy of high intensity interval training in type 2 diabetes. *Diabetes Res Clin Pract* 2013;99:120–9. doi:10.1016/j.diabres.2012.10.019.
- [32] Zaharieva DP, Riddell MC. Insulin management strategies for exercise in diabetes. *Can J Diabetes* 2017;42:507-516. doi: 10.1016/j.jcjd.2017.07.004.
- [33] Marliss EB, Vranic M. Intense exercise has unique effect on both insulin release and its role in glucoregulation. *Diabetes* 2002;51:271-283. doi: 10.2337/diabetes.51.2007.S271.

Highlights

- Simple self-testing methods could be used to measure improvements after 8 times of HIT
- HIT improved 2h blood glucose concentration, diastolic blood pressure and weight
- HIT was well-tolerated, and no adverse events were recorded

ACCEPTED MANUSCRIPT