ORIGINAL ARTICLE

Gender-dependent evaluation of football as medicine for prediabetes

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Abstract

Purpose Training intensity and health effects of football were investigated gender specifically in individuals with prediabetes.

Methods Participants with prediabetes (age 60 ± 6 years) were randomised into a football and dietary advice group (FD-men $n = 13$ and FD-women $n = 14$) or a dietary advice only group (D-men $n = 12$ and D-women $n = 11$). FD performed football training (twice/week for 16 weeks), while both groups received dietary advice. Body composition, bone variables, blood pressure, blood lipid profile and peak oxygen uptake (VO_{2peak}) were determined pre- and post-intervention.

Results Mean heart rate during football training was 79 ± 2 and $80 \pm 3\%$ HR_{max} for FD-men and FD-women, respectively, with peak heart rate values of 96 ± 1 and $97 \pm 2\%$ HR_{max}, with no gender differences. VO_{2peak} increased more ($P < 0.05$) in FD-men and FD-women than in D-men and D-women. However, relative delta change in VO_{2peak} was $21 \pm 14\%$ in FD-women, which was greater ($P < 0.05$) than in FD-men ($11 \pm 12\%$). Reduction in SBP and DBP, respectively, was similar in FD-men (-10.8 ± 13.0 and -7.3 ± 11.8 mmHg) and FD-women (-11.3 ± 11.0 and -7.1 ± 6.2 mmHg), with within-gender differences for men. Total plasma cholesterol and LDL cholesterol decreased ($P < 0.05$) by -0.7 ± 1.1 and -0.5 ± 0.9 mmol L^{-1}, respectively, in FD-women and -0.2 ± 0.4 and -0.2 ± 0.3 mmol L^{-1} in FD-men, with no significant gender differences ($P = 0.08$). Body fat content was lowered ($P < 0.05$) by 3 and 4%-points in FD-men and FD-women, respectively.

Conclusion Gender-mixed football training combined with dietary advice causes broad-spectrum health effects for men and women with prediabetes, with minor gender-specific differences. Thus, the intensity and training-induced effects of football training are also high for elderly women with prediabetes.

Keywords Soccer · VO_{2peak} · Fat percentage · Blood pressure · Cholesterol · Cardiometabolic fitness

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Abbreviations

ANOVA	Analysis of variance
BTM	Bone turnover markers
BMC	Bone mineral content
BP	Blood pressure
CI	Confidence interval
CRP	C-reactive protein
CTX	C-terminal telopeptide
BMD	Bone mineral density
DBP	Diastolic blood pressure
Diet-men	Diet men
Diet-women	Diet women
DXA	Dual-energy X-ray absorptiometry
ES	Effect size
FD-men	Football and diet men
FD-women	Football and diet women
HR	Heart rate
HDL	High-density lipoprotein
IFG	Impaired fasting glycaemia
IGT	Impaired glucose tolerance

LBM	Lean body mass
LDL	Low-density lipoprotein
L2, L3 and L4	Lumbar vertebrae
MAP	Mean arterial pressure
OGTT	Oral Glucose Tolerance Test
VO_{2peak}	Peak oxygen uptake
P1NP	Procollagen type I N propeptide
RCT	Randomized Controlled Trial
RHR	Resting heart rate
SD	Standard deviation
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides
T2DM	Type II diabetes mellitus
VO_{2max}	Maximal oxygen uptake
W	Watt

Introduction

Impaired glycaemic control leads, if left untreated, to type 2 diabetes mellitus (T2DM), which is one of the most comprehensive health challenges worldwide, causing considerable morbidity and mortality in men and women (Yang et al. 2017). Based on the recent epidemiological data, the International Diabetes Federation (IDF) has estimated that the global prevalence of T2DM and prediabetes among adults aged 18–99 years totals 451 million incidents, with a higher prevalence among men than women. In high-income countries, the prevalence peaks among 75−79 year olds and, notably, the estimated worldwide prevalence of prediabetes is 374 million cases, corresponding to 8% of the world's population (Cho et al. 2018).

T2DM is believed to develop in both gender through a progressive impairment in glucose regulation known as prediabetes, characterized by impaired fasting glycaemia (IFG), impaired glucose tolerance (IGT) or both (Jagannathan and Bergman 2017). However, patients with manifested T2DM or prediabetes additionally have a higher prevalence of other serious health complications, such as poor physical fitness, obesity and several cardiovascular deficiencies (Flores-Le Roux et al. 2011). Thus, there is a need for broad-spectrum treatment for these specific patient groups, with exercise training combined with nutritional therapy being the cornerstone of the approach for both genders with prediabetes and T2DM (Pedersen and Saltin 2015).

Gender-based differences in substrate metabolism during exercise have been well established. Specifically, during moderate-intensity endurance exercise, women display lesser reliance on whole-body glycogen breakdown as well as protein and carbohydrate oxidation to fuel energy requirements during exercise in comparison to men (Devries et al. 2006; Phillips et al. 1993; Tarnoplosky et al. 1990).

Moreover, during high-intensity exercise women utilise up to 50% less muscle glycogen during the exercise bout compared their male counterparts (Esbjörnson-Liljedahl et al. 1999). These gender-specific differences may ultimately influence the adaptive response to prolonged exercise training. For example, Metcalfe et al. (2012) demonstrated that women may have an inferior adaptive capacity in blood glucose regulation compared to men after a 6-week high-intensity training protocol, despite the same increase in maximal oxygen uptake (VO_{2max}). Moreover, women demonstrate less skeletal muscle hypertrophy after high-intensity training than men (Scalzo et al. 2014), as well as a different and less favourable fat reduction pattern after an intervention period combining strength exercises at moderate intensities with aerobic training (Sanal et al. 2013). Thus, gender differences may exist in some physiological variables for certain types of exercise training.

Women with diabetes appear to have poorer control of modifiable risk factors (Gouni-Berthold et al. 2008) and more difficulty reaching their treatment targets than men (Kautsky-Willer et al. 2010). This underlines the need for new, attractive and health-beneficial modes of physical activity to be introduced to the female population together with dietary advice and well-regulated medical treatment. In a recent meta-analysis review, football training was shown to be broad-spectrum medicine for both genders (Milanovic et al. 2018). Thus, the potential gender differences in adaptation to exercise training discussed above may be less when a complex and broad-spectrum training approach is applied. The training concept has been tested in sedentary healthy individuals (Krustrup et al. 2010a, b; Bangsbo et al. 2010), elderly subjects (Helge et al. 2014a, b) and patients with various chronic conditions, such as arterial hypertension (Mohr et al. 2014) and type 2 diabetes (de Sousa et al. 2014). However, the Football Fitness concept has so far been investigated in isolation in men (Krustrup et al. 2009, 2010a, b, 2013; Uth et al. 2014, 2016a, b; Helge et al. 2014a, b) and women (Krustrup et al. 2010a, b, 2018; Barene et al. 2013) during training with no studies having applied mixed-gender football training to a participant group with multiple health challenges.

Recently, we tested the application of the Football Fitness concept at national level in the Faroe Islands (av Fløtum et al. 2016). All adults in the country were given the opportunity to take part in the exercise intervention, but 85% of the participants volunteering were women (av Fløtum et al. 2016). Thus, it is of interest to comprehensively examine whether the Football Fitness concept, together with standardized dietary advice, can be successfully applied to a mixed-gender setting in a relatively frail participant group with several health challenges.

The purpose of the present study was, therefore, to test the hypothesis that football training organised as mixed-gender

training causes similar broad-spectrum health benefits in men and women with prediabetes aged 55–70 years.

Materials and methods

Participants

The participants originated from a population-based cross-sectional survey, which determined the prevalence of T2DM and prediabetes among the population aged 40–74 years in the Faroe Islands. The sample comprises 1772 individuals, corresponding to ~10% of the entire population aged 40–74 years (Veyhe et al. 2018). T2DM and prediabetes were determined by a diagnostic algorithm, including HbA1c, fasting plasma glucose and an OGTT (see Veyhe et al. 2018, 2019).

In total, 117 individuals aged 55–70 years diagnosed with prediabetes based on Veyhe et al. (2018) were approached by the research group with a view to participation in the study. The participants that took part in regular physical activity and individuals using beta-blockers were excluded from participation. In contrast, participants using other antihypertensive drugs such as thiazides and angiotensin receptor blockers ($n = 25$) were included. In addition, participants taking medication for high plasma cholesterol levels such as statins ($n = 16$) were included. Finally, three participants included in the study were taking anti-asthmatic drugs (glucocorticoids and β2-receptor agonists). None of the participants changed their drug administration during the intervention period. After being informed of the experimental procedures and associated risks, 55 individuals (28 men and 27 women; see Table 1) volunteered to participate in the study

and gave their written consent. Power calculations of the primary endpoint revealed that 10–15 participants in each group are sufficient to show potential between-group differences using an ANOVA approach. The study was approved by the ethical committee of the Faroe Islands and conducted in accordance with the Declaration of Helsinki (1964). Data from the entire sample have previously been presented by Skoradal et al. (2018a, b).

Experimental design

The experimental design was a gender-specific randomized controlled trial. The participants reported to the laboratory on four separate occasions over a 12-day period. On visit 1, a fasting blood sample was drawn and an oral glucose tolerance test (OGTT) conducted, as described by Connolly et al. (2016). Moreover, blood pressure and resting heart rate were recorded. On visit 2, body composition was determined with a DXA scan, scaling body mass and measuring waist and hip circumference, as previously described (Kharal et al. 2013). On visit 3, the participants performed an incremental cycling test to exhaustion with measurement of peak oxygen uptake (VO_{2peak}) and maximal heart rate (HR_{max}). The primary endpoints were HR loading during training, blood lipid profile and glucose, body composition, blood pressure and VO_{2peak}, while the secondary endpoints were body mass, resting heart rate, bone mineral content, bone mineral density, blood markers of bone turnover, and waist and hip circumference. On visit 4, dietary advice was given by a registered dietician in a 3-h group session. Subsequently, the participants were randomised gender specifically to a football and dietary advice group (FD; $n = 32$) and a dietary advice group (D; $n = 23$). Men and women were

Table 1 Participant characteristics at baseline

	FD-men ($n = 13$)	FD-women ($n = 14$)	D-men ($n = 12$)	D-women ($n = 11$)
Age (years)	62 ± 5	57 ± 5	61 ± 6	63 ± 6
Height (cm)	178 ± 6*	166 ± 4	178 ± 6*	163 ± 6
Weight (kg)	91 ± 15*	77 ± 11	96 ± 20*	83 ± 13
Body fat (%)	28 ± 5*	43 ± 3	31 ± 5*	47 ± 4
LBM (kg)	63.1 ± 6.1*	43.6 ± 6.0	64.7 ± 11.7*	43.0 ± 4.8
Hip circumference (cm)	98 ± 10*	106 ± 8	101 ± 10*	110 ± 9
Waist circumference (cm)	97 ± 6	101 ± 7	103 ± 8	108 ± 10
VO_{2max} (mL min^{-1} kg^{-1})	28.0 ± 5.2*[#]	22.1 ± 3.4[#]	20.7 ± 5.5*	18.7 ± 3.0
MAP (mmHg)	105.2 ± 9.1*	97.1 ± 7.7[¤#]	101.8 ± 14.0*	107.1 ± 9.3

Age, body composition, maximal oxygen uptake and mean arterial pressure of men and women in the football and diet intervention (FD) and diet intervention (D). Data are means ± SD

*Significant difference from their gender counterparts

[#]Significant difference from the gender-specific intervention counterpart,

[¤]Significant difference from all other groups

Significance level $P < 0.05$

randomised separately to ensure an equal gender distribution in the two groups. There were five drop outs from the FD group (due to low training attendance; < 1 session per week, which was the minimum criterion for training completion), of which two were men and three were women, resulting in 27 participants completing the FD intervention (FD-men $n = 13$; FD-women $n = 14$). There were no dropouts from D ($n = 23$; D-men $n = 12$, D-women $n = 11$). Thus, the final sample consisted of 50 participants. There were examples of severe muscle soreness as a result of the football training in the initial phase of the intervention period, but no serious injuries occurred.

Training intervention

In FD, men and women trained together. FD completed a total of 32 ± 5 (19–46) football training sessions over the 16-week intervention period, corresponding to 2.0 ± 0.3 (1.2–2.9) sessions per week, with no difference between genders. Four training sessions were organised per week, and the participants were encouraged to take part in 2–3 sessions per week. Each session lasted 30–60 min (30 min during weeks 0–2, 40 min during weeks 3–4, 50 min during weeks 5–6 and 60 min during weeks 7–16). The sessions were organised in two halves separated by 2–3 min of recovery). All sessions were organised as small-sided games (4v4–6v6), as previously described (Randers et al. 2010). All sessions were preceded by a 10-min warm-up period (Mohr et al. 2014). Heart rate was measured during one training session in week 4 and one session in week 12 of the intervention. Heart rate was recorded in 5-s intervals throughout the training sessions with a Polar Vantage NV monitor (Polar Electro Oy, Kempele, Finland). Maximal heart rate (HR_{max}) was assessed during the exhaustive bike test.

Dietary intervention

Both intervention groups took part in group-based dietary advice sessions led by a registered dietician and provided with a standardised meal plan. The meal plan aimed to improve glycaemic control, reduce the risk of worsening cardiometabolic profile and maintain healthy body weight. Weight loss in diabetic individuals may provide clinical benefits such as improved glycaemia, blood pressure and lipids (American Diabetes Association 2017). Thus, the meal plan was semi-low-caloric, providing 1800 and 2300 kcal per day for the women and men, respectively. Previous studies of group-based diabetes education have reported HbA1C decreases of 0.5–2.0% in T2DM patients (American Diabetes Association 2017). The main principles of the meal plan were substituting high-starch and high-sucrose foods with low-glycaemic natural fibre-rich plant foods (Wheeler et al. 2012). In accordance with the official Danish dietary

recommendations, the recommended vegetable intake was 300 g per day and fruit consumption was limited to two to three pieces per day in order to limit fructose intake (Wheeler et al. 2012; Danish Veterinary and Food Administration 2013). The participants were instructed to minimise consumption of sucrose-containing foods, especially sugar-sweetened beverages and to substitute starchy foods with wholemeal foods such as wholemeal bread, pasta and rice (Nordic Council of Ministers 2012). The recommended intake of saturated fat, dietary cholesterol and trans fat is the same for diabetic subjects as for the healthy population (American Diabetes Association 2017; Nordic Council of Ministers 2012). However, based on Danish dietary surveys, the participants were advised to increase consumption of foods containing long-chain n-3 fatty acids (EPA and DHA) from fatty fish (Nordic Council of Ministers 2012).

Dual-energy X-ray absorptiometry (DXA) scanning

Whole-body fat and lean body mass (LBM) were evaluated by total-body DXA scanning (Norland XR-800, Norland Corporation, Oslo, Norway). The body was segmented in accordance with the standard procedures to evaluate regional tissue distribution and all analyses were performed using Illuminatus DXA software (Norland Corporation, Oslo, Norway). The effective radiation dose was < 0.2 mSv per scan. Additionally, site-specific scans of the lumbar spine and proximal femur were conducted as previously described (Mohr et al. 2015). BMC and BMD in the lumbar vertebrae L2, L3 and L4, and in the femoral neck, trochanter and shaft were evaluated. The coefficient of variation of test–retest measurements of the specific DXA scanner applied on the main outcome variables is 1.2–1.5%.

Resting blood sampling and OGTT testing

On the day of testing, the participants reported to the laboratory after transport by car or bus. No training was performed 48–72 h prior to testing and the participants were instructed to avoid physical activity on the day prior to the OGTT tests. Using a venipuncture technique, a resting blood sample was taken under standardised conditions from an antecubital vein between 7 a.m. and 8 a.m. after an overnight fast. The blood was rapidly centrifuged for 30 s and the plasma collected and analysed by an automatic analyzer (Cobas Fara, Roche, France) using enzymatic kits (Roche Diagnostics, Germany) to determine plasma total cholesterol, HDL, LDL, triglycerides, C-reactive protein and vitamin D. Additionally, an OGTT test was performed as previously described (Durrer et al. 2015), with blood samples taken after 0, 30, 60 and 120 min and analysed for plasma [glucose] using enzymatic kits (Roche Diagnostics, Germany). The intra-assay coefficient of variations for glucose is $3.0 \pm 3.5\%$. Finally, the

remaining plasma samples were frozen and subsequently analysed for bone turnover markers (BTM), i.e. procollagen type I N propeptide (P1NP), osteocalcin and C-terminal telopeptide (CTX), using ELISA and AlphaLISA apparatus (PerkinElmer, Cambridge, United Kingdom) at the scientific laboratory at the Research Center for Ageing and Osteoporosis, Departments of Diagnostics and Medicine, Copenhagen University Hospital Glostrup, Glostrup, Denmark.

Blood pressure measurements and resting heart rate

The participants reported at the hospital at 8.00 a.m. after an overnight fast and rested in a supine position for 2 h. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the standard procedures (Krustrup et al. 2013) using an automatic BP monitor (HEM-709; OMRON, IL, US) once every 30 min over the 2-h resting period. The average of the four measurements was the test result. Mean arterial pressure (MAP) was calculated as 1/3 SBP + 2/3 DBP. Resting heart rate (RHR) was determined during the same time intervals as for blood pressure.

Peak oxygen uptake

On a separate day, the participants reported to the laboratory in a post-absorptive state (at least 4 h), having refrained from vigorous exercise, alcohol, tobacco and caffeine during the previous 24 h. To ensure standardisation of nutritional and hydration status, the participants recorded their food and fluid intakes for the 48-h period prior to the first trial so that the diet could be repeated for the remainder of the trial. The participants did not consume any fluid during the experimental trials. Peak oxygen consumption (VO_{2peak}) was determined for each individual by means of an incremental cycling test to volitional exhaustion on an electromagnetically braked cycle ergometer (Excalibur Sport, Lode, Groningen, The Netherlands). The test was performed under standard laboratory conditions (20 °C; 40% relative humidity). VO_{2peak} was determined as the highest value achieved over a 20-s period. A plateau in VO_2, with an increase in VO_2 of less than 0.5 ml/min/kg despite an increased bicycle test loading by 20 W, and a respiratory exchange ratio (RER) > 1.15 were used as criteria for VO_{2peak} achievement. The test was initiated at 0 W and increased by 20 W every minute until the point of volitional exhaustion. The participants maintained a cadence of 60, 65 or 70 rep min^{-1} based on individual preference. Pulmonary VO_2 was measured throughout the protocol by a breath-by-breath gas analysing system (model Cosmed, Quark b2, Milan, Italy). The analyzer was calibrated before each test with two gases of known oxygen and carbon dioxide concentrations as well as by the use of a 3-l syringe for the tube flowmeter calibration.

Maximal heart rate (HR$_{max}$) was additionally determined during the exhaustive bike test as the peak value reached in a 5-s interval.

Statistical analysis

Data are presented as means ± SD. Statistical analyses were performed using SPSS v.22. A two-factor mixed ANOVA design with the between-factor 'group' and repeated factor 'condition' (pre- vs post-intervention) was used. When significant main effects were detected, data were subsequently analysed using Bonferroni post hoc t tests. The significance level was $P < 0.05$.

Results

Baseline differences

Baseline VO_{2peak} was higher ($P < 0.05$) in FD-men and FD-women compared to their gender counterparts in D (Table 1). Baseline SBP was lower ($P < 0.05$) in FD-women than in any of the other groups, and DBP in FD-women at baseline was lower ($P < 0.05$) than in D-women (Fig. 4). Total cholesterol at baseline was lower ($P < 0.05$) in D-men compared to D-women and FD-women, while LDL cholesterol was lower ($P < 0.05$) in D-men than in all other groups (Table 2). The FD group had lower plasma glucose levels at some time points (60 and 120 min) than their gender-specific D-group (Table 2). Baseline body fat content was lower ($P < 0.05$) in FD-men and D-men than in their female counterparts (Table 1). Baseline whole-body BMC and BMD and in site-specific skeletal regions were similar between FD-men and D-men, as well as between FD-women and D-women (Table 3).

Training responses

Mean and peak heart rates were 128 ± 5 and 155 ± 6 bpm, respectively, corresponding to 80 ± 3 and 97 ± 2% HR$_{max}$, respectively. No gender differences were observed in mean heart rate (FD-men 79 ± 2% HR$_{max}$, FD-women 80 ± 3% HR$_{max}$) or peak heart rate response (FD-men 96 ± 1% HR$_{max}$, FD-women 97 ± 2% HR$_{max}$, Fig. 1).

Body composition

All four groups had a lowering of body weight during the intervention (FD-men; 1.9 ± 1.7 kg, FD-women; −2.8 ± 3.4 kg, D-men; 1.3 ± 3.0 kg, D-women; 1.8 ± 3.5 kg), with no between-group differences. Waist circumference was reduced ($P < 0.05$) by 4.3 ± 2.9 and 5.3 ± 4.0 cm in FD-men and FD-women, respectively, with no change in

Table 2 Plasma parameters pre- and post-intervention

	FD-men		FD-women		D-men		D-women	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
TC (mmol L^{-1})	5.3 ± 0.9	5.1 ± 0.9*	5.7 ± 0.7	5.0 ± 1.1*§	4.3 ± 1.2¤	4.3 ± 1.0¤	5.7 ± 1.0	5.7 ± 1
HDL (mmol L^{-1})	1.4 ± 0.3	1.4 ± 0.3	1.5 ± 0.2	1.4 ± 0.3	1.3 ± 0.5	1.2 ± 0.3	1.6 ± 0.3	1.6 ± 0.3
LDL (mmol L^{-1})	3.4 ± 0.9	3.2 ± 0.9*§	3.6 ± 0.6	3.1 ± 0.9*	2.4 ± 0.9	2.6 ± 0.6	3.5 ± 1.0	3.5 ± 0.9
TG (mmol L^{-1})	1.3 ± 0.7	1.2 ± 0.2	1.4 ± 0.5	1.2 ± 0.4	1.6 ± 1.3	1.3 ± 0.9	1.3 ± 0.5	1.4 ± 0.4
CRP (mg L^{-1})	4.3 ± 4.6	4.2 ± 4.8	3.4 ± 4.3	3.2 ± 3.7	4.2 ± 5.1	3.7 ± 5.7	3.4 ± 1.8	2.8 ± 2.2
Vitamin D (nmol^{-1})	59.2 ± 29.8	63.9 ± 31.5	64.9 ± 25.6	62.4 ± 24.6	59.0 ± 29.4	56.0 ± 27.2	52.4 ± 19.1	52.1 ± 16.6
Oral Glucose Tolerance Test (OGTT)								
Glucose (mmol L^{-1})								
0 min	6.4 ± 0.8	6.0 ± 0.6*	6.1 ± 0.7	5.7 ± 0.5*	6.0 ± 0.8	5.8 ± 0.8*	6.5 ± 0.8	5.9 ± 0.6*
30 min	10.6 ± 2.1	10.6 ± 2.0	9.5 ± 1.4	9.1 ± 1.3	10.2 ± 1.1	9.7 ± 1.5	10.8 ± 1.7	10.5 ± 2.2
60 min	11.5 ± 3.3	9.7 ± 2.9*	9.8 ± 3.2#	8.3 ± 2.4*#	11.6 ± 3.4	9.4 ± 3.0*	12.9 ± 1.9	11.9 ± 2.1*
120 min	7.5 ± 2.5#	5.1 ± 1.2*#	7.2 ± 2.3#	6.2 ± 1.7*#	9.3 ± 4.2	7.4 ± 3.0*	9.4 ± 2.4	7.6 ± 1.6*

Plasma lipid profile (total cholesterol (TC), HDL, LDL, triclycerides (TG), C-reactive protein (CRP) and vitamin D, as well as glucose at 0, 30, 60 and 120 min during the oral glucose tolerance test in FD-men ($n = 13$), FD-women ($n = 14$), D-men ($n = 12$) and D-women ($n = 11$). Data are mean $\pm$ SD

*Significant difference from corresponding values pre-intervention

§Significant difference in change score from gender counterparts

#Significant difference in absolute value from gender-specific group in D

¤Significant difference from all other groups

Significance level $P < 0.05$

the D-groups (D-men 3.0 ± 4.7; D-women 0.7 ± 4.1 cm). Total body fat content was lowered ($P < 0.05$) during the intervention period from 28 ± 5 to 25 ± 7% in FD-men and from 43 ± 3 to 39 ± 4% in FD-women, respectively, with no change score difference. The reduction in fat mass was 2.8 ± 2.2 and 4.0 ± 3.5 kg in FD-men and FD-women, respectively, with no gender differences. However, the change score in fat mass was greater ($P < 0.05$) than in their gender-specific counterparts in the D intervention (D-men 1.1 ± 3.0 and D-women 1.3 ± 2.0 kg). The intervention-induced decrement ($P < 0.05$) in fat mass in the D groups did not affect body fat percentage in either D-men (pre 31 ± 5, post 30 ± 5%) or D-women (pre 47 ± 4, post 46 ± 3%), and no gender-specific between-group differences were observed (Fig. 2). LBM increased ($P < 0.05$) during the intervention in FD-men (0.59 ± 1.04 kg) and FD-women (0.74 ± 1.80 kg), with greater change scores ($P < 0.05$) than in their gender-specific counterparts (D-men -0.29 ± 1.35 kg, D-women 0.31 ± 1.77 kg; Fig. 2).

Lipid profile and blood glucose

Total plasma cholesterol was lowered ($P < 0.05$) by 0.7 ± 1.1 mmol L^{-1} in FD-women (Fig. 3), while FD-men tended ($P = 0.08$) to have lower total plasma cholesterol post-intervention (-0.2 ± 0.4 mmol L^{-1}). The

change score was greater ($P < 0.05$) in FD-women than in D-women, with no difference between the male groups (Fig. 3). Plasma LDL cholesterol was reduced ($P < 0.05$) in both FD-men and FD-women (-0.2 ± 0.3 and -0.5 ± 0.9 mmol L^{-1}, respectively) post-intervention (Fig. 3). The change score in FD-men was greater ($P < 0.05$) than that in D-men ($+0.2 \pm 0.3$ mmol L^{-1}), while FD-women did not differ from D-women (0.0 ± 0.5 mmol L^{-1}). There were no between- or within-group differences for plasma HDL cholesterol or triglyceride (Table 2).

Resting blood glucose was lowered ($P < 0.05$) post-intervention in all four groups (Table 2). After 60 min of OGTT, blood glucose was also lower ($P < 0.05$) post-intervention in all groups, with no difference in change score between groups (Table 2). At the 120-min time point, all four groups had lower ($P < 0.05$) blood glucose values post-intervention compared to baseline (Table 2). The absolute blood glucose values were lower at the 120-min time point in FD-men and FD-women (5.1 ± 1.2 and 6.2 ± 1.7 mmol L^{-1}, respectively) compared to their gender-specific counterparts (D-men 7.4 ± 3.0 and D-women 7.6 ± 1.6 mmol L^{-1}; Table 2). Moreover, FD-men had lower ($P < 0.05$) post-intervention 120-min plasma glucose concentrations in comparison to FD-women.

Table 3 Bone mineral content (BMC) and density (BMD) pre- and post-intervention

	FD-men		FD-women		D-men		D-women	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Femur neck								
BMC (g)	3.17 ± 0.41	$3.22 \pm 0.43*$	2.82 ± 0.37	2.85 ± 0.35	3.49 ± 0.63	3.51 ± 0.63	2.82 ± 0.50	2.84 ± 0.53
BMD (g cm^{-2})	0.82 ± 0.11	$0.84 \pm 0.11*^{\#}$	0.85 ± 0.12	$0.89 \pm 0.14*^{\#}$	0.93 ± 0.18	0.93 ± 0.19	0.84 ± 0.12	0.85 ± 0.13
Femur shaft								
BMC (g)	17.9 ± 2.4	18.1 ± 2.4	16.2 ± 2.2	17.1 ± 2.1	18.9 ± 4.4	18.9 ± 4.2	16.0 ± 2.1	16.0 ± 2.5
BMD (g cm^{-2})	1.02 ± 0.13	$1.06 \pm 0.12*^{\#}$	1.03 ± 0.13	$1.05 \pm 0.13*^{\#}$	1.09 ± 0.21	1.08 ± 0.20	1.00 ± 0.14	0.99 ± 0.14
Femur trochanter								
BMC (g)	14.8 ± 2.2	$15.2 \pm 2.8^{\#}$	9.9 ± 2.3	10.2 ± 2.1	14.3 ± 5.0	$13.8 \pm 5.0*$	9.0 ± 2.4	8.9 ± 2.4
BMD (g cm^{-2})	0.78 ± 0.11	0.79 ± 0.11	0.71 ± 0.12	0.73 ± 0.17	0.82 ± 0.20	0.81 ± 0.20	0.70 ± 0.13	0.69 ± 0.14
Vertebrae L2								
BMC (g)	17.9 ± 4.5	18.7 ± 4.8	15.5 ± 1.5	15.5 ± 1.8	20.0 ± 4.6	19.9 ± 4.7	13.6 ± 2.8	13.4 ± 2.7
BMD (g cm^{-2})	1.06 ± 0.16	1.06 ± 0.17	1.04 ± 0.09	$1.08 \pm 0.09*^{\#}$	1.18 ± 0.21	1.18 ± 0.19	0.90 ± 0.17	0.91 ± 0.16
Vertebrae L3								
BMC (g)	18.9 ± 2.9	19.2 ± 2.7	16.6 ± 2.5	17.2 ± 2.9	22.2 ± 5.2	21.6 ± 4.8	14.9 ± 3.9	15.2 ± 4.0
BMD (g cm^{-2})	1.08 ± 0.14	$1.13 \pm 0.20*^{\#}$	1.05 ± 0.14	1.07 ± 0.15	1.22 ± 0.24	1.21 ± 0.22	0.92 ± 0.18	0.94 ± 0.20
Vertebrae L4								
BMC (g)	20.6 ± 4.8	21.2 ± 5.2	18.2 ± 3.1	18.2 ± 2.6	24.8 ± 6.8	24.2 ± 6.3	16.0 ± 3.6	15.6 ± 3.5
BMD (g cm^{-2})	1.06 ± 0.15	1.08 ± 0.15	1.09 ± 0.12	1.11 ± 0.13	1.30 ± 0.37	1.30 ± 0.36	0.93 ± 0.17	0.92 ± 0.14

Bone mineral content (BMC) and bone mineral density (BMD) in sites in the proximal femur and lumbar spine in FD-men ($n = 13$), FD-women ($n = 14$), D-men ($n = 12$) and D-women ($n = 11$). Data are mean $\pm$ SD

*Significant difference from corresponding values pre-intervention

§Significant difference in change score from gender counterparts

#Significant difference from gender-specific group in D

Significance level $P < 0.05$

Blood pressure and resting heart rate

All groups had reductions in SBD and DBP during the intervention, except D-men (Fig. 4). In FD, the reductions in systolic and diastolic blood pressure, respectively, were similar in men (FD-men -10.8 ± 13.0 and -7.3 ± 11.8 mmHg) and women (FD-women -11.3 ± 11.0 and -7.1 ± 6.2 mmHg), although it should be noted that within-gender differences were only seen for men, with no effect on systolic and diastolic blood pressure in D-men (1.6 ± 14.7 and 0.4 ± 9.2 mmHg). D-women displayed a similar decline (10.7 ± 10.6 and 8.5 ± 9.5 mmHg, $P < 0.05$) to FD-women (Fig. 4). FD-men and FD-women had a similar reduction in MAP, which gender specifically was greater ($P < 0.05$) than in D-men but similar to D-women (Fig. 4). RHR was lowered ($P < 0.05$) post-intervention in FD-men and FD-women (-5 ± 6 and -4 ± 9 bts min^{-1}, respectively), with no change in either D-men or D-women (1 ± 4 and 1 ± 6 bts min^{-1}, respectively).

Peak oxygen uptake

FD-men and FD-women improved their VO_{2peak} more (2.6 ± 2.7 and 4.4 ± 2.2 mL min^{-1} kg^{-1}, respectively; $P < 0.05$) than D-men and D-women (0.7 ± 2.6 and 0.2 ± 2.0 mL min^{-1} kg^{-1}; Fig. 5) post-intervention. No gender difference was observed in change scores in either intervention group in absolute values; however, the percentage change in peak oxygen uptake was $21 \pm 14\%$ in FD-women, which was greater ($P < 0.05$) than that in FD-men ($11 \pm 12\%$).

Bone mineral content and density

FD-men increased ($P < 0.05$) BMC by $1.8 \pm 3.1\%$ in the femur neck during the intervention, with no between-group differences from FD-women (Table 3). Femur neck and shaft BMD were increased ($P < 0.05$) in both FD-men (2.5 ± 2.7 and $3.4 \pm 6.0\%$, respectively) and FD-women (3.9 ± 3.2 and $1.8 \pm 1.8\%$, respectively) during the intervention, and with

Fig. 1 Training responses. Mean (**a**) and peak (**b**) heart rate and relative mean (**c**) and peak (**d**) heart rate during a football training session in FD-men and FD-women. Mean (broken line) and individual values are presented
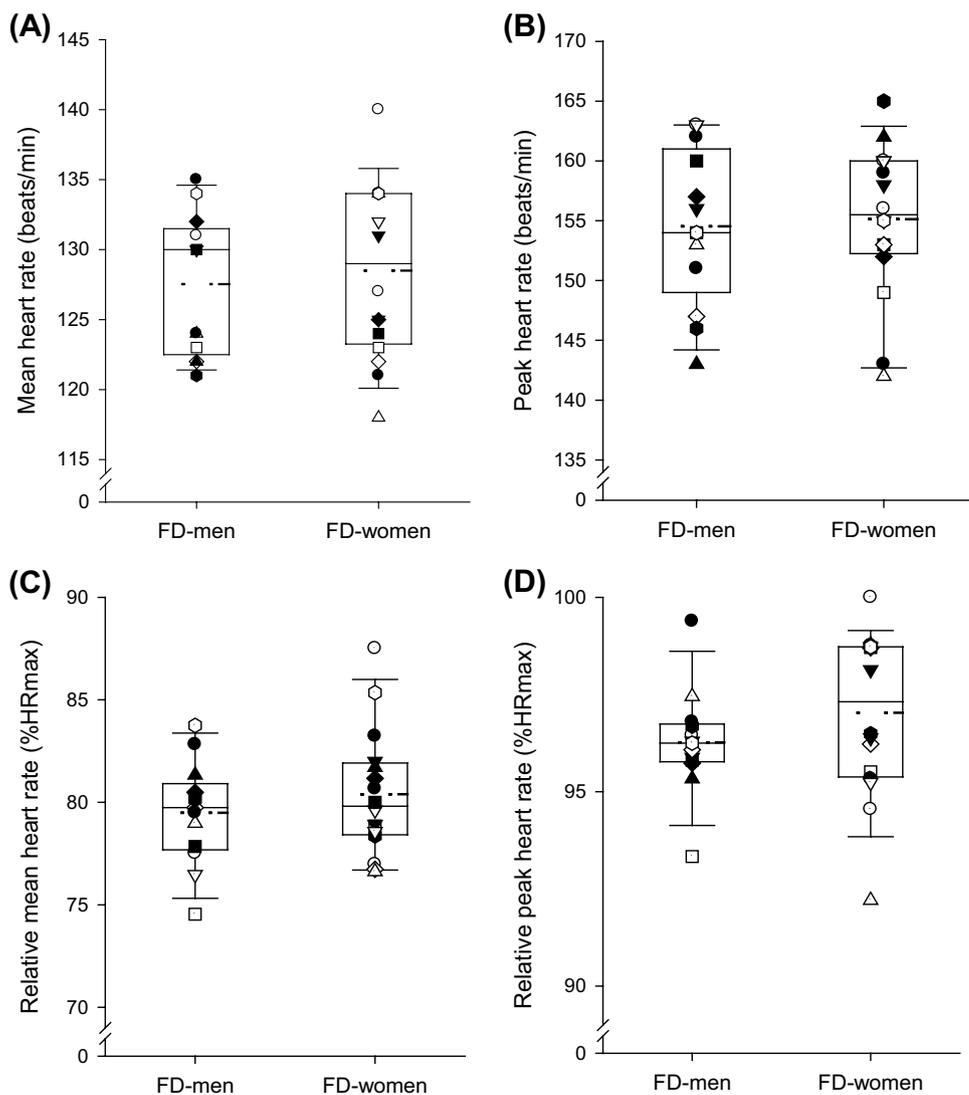
greater ($P < 0.05$) gender-specific change scores compared to D-men (0.3 ± 2.7 and $-1.4 \pm 2.4\%$, respectively) and D-women (0.7 ± 2.8 and $-0.9 \pm 2.5\%$, respectively; Table 3). In addition, in FD-men BMD was increased ($P < 0.05$) in L3 ($4.1 \pm 6.2\%$), with a greater ($P < 0.05$) change score than in D-men ($-0.8 \pm 2.8\%$). In FD-women, BMD was improved ($P < 0.05$) in L2 ($3.9 \pm 5.7\%$), which was also greater than the delta change in D-women ($1.6 \pm 2.8\%$). D-men displayed a decrease ($P < 0.05$) in femur trochanter BMC and femur shaft BMD during the intervention period, while D-women displayed a decrease ($P < 0.05$) in L3 BMC and BMD (Table 3).

Bone turnover markers

Both FD groups experienced similar increased ($P < 0.05$) plasma osteocalcin, P1NP and CTX-1 during the intervention (FD-men 38.1 ± 34.0, 58.3 ± 33.1 and $27.1 \pm 37.1\%$;

FD-women 37.4 ± 41.5, 46.0 ± 57.5 and $19.9 \pm 47.3\%$, respectively) with greater ($P < 0.05$) increases than in their gender-specific counterparts (Table 3).

Discussion

The principal findings of the present study were that 16 weeks of treatment with gender-mixed football training and dietary advice cause broad-spectrum health effects in both men and women aged 55–70 years with prediabetes. The improvements in cardiovascular, metabolic and bone health were similar in men and women, with only minor gender-specific differences and markedly greater for both genders than with dietary advice treatment alone.

The broad-spectrum health benefits observed in the present study are consistent with the large number of studies using football training for prevention and treatment of
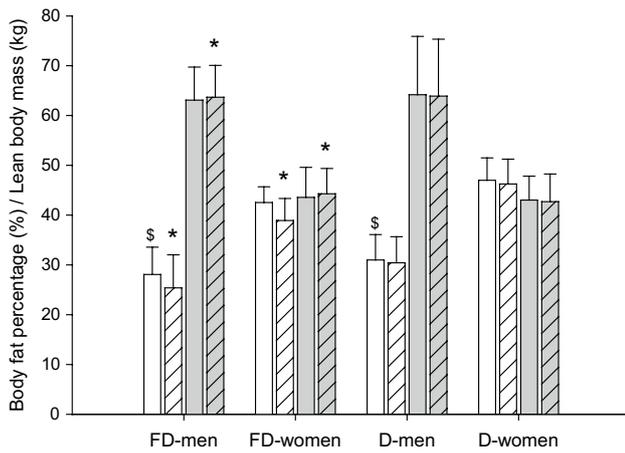
Fig. 2 Body composition. Total body fat percentage before (open bars) and after (open/hatched bars) as well as lean body mass before (grey bars) and after (grey/hatched bars) the intervention in FD-men, FD-women, D-men and D-women. *($P < 0.05$) different from before the intervention. $^\$$Different ($P < 0.05$) from female counterparts at baseline
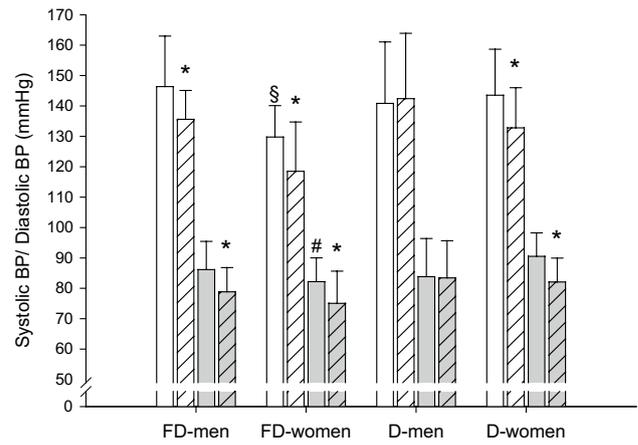

Fig. 4 Blood pressure. Systolic blood pressure (BP) before (open bars) and after (open/hatched bars) as well as diastolic BP before (grey bars) and after (grey/hatched bars) the intervention in FD-men, FD-women, D-men and D-women. *($P < 0.05$) different from before the intervention. §($P < 0.05$) different from all other groups at baseline. Significantly ($P < 0.05$) different from D-women at baseline
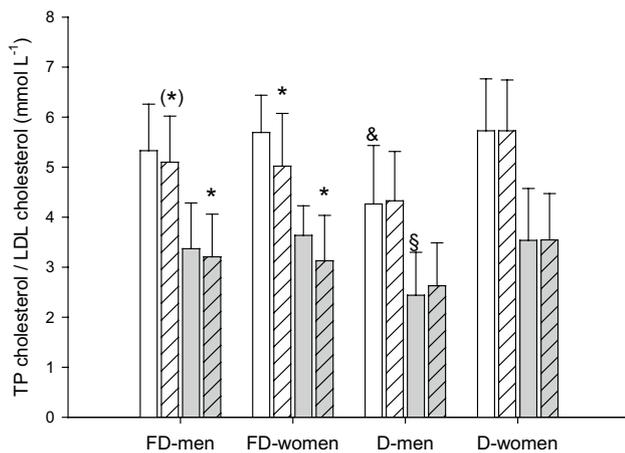
Fig. 3 Lipid profile. Total plasma (TP) cholesterol before (open bars) and after (open/hatched bars) as well as LDL cholesterol before (grey bars) and after (grey/hatched bars) the intervention in FD-men, FD-women, D-men and D-women. *($P < 0.05$) different from before the intervention. $^\&$Different ($P < 0.05$) from FD-women and D-women at baseline. §($P < 0.05$) different from all other groups at baseline
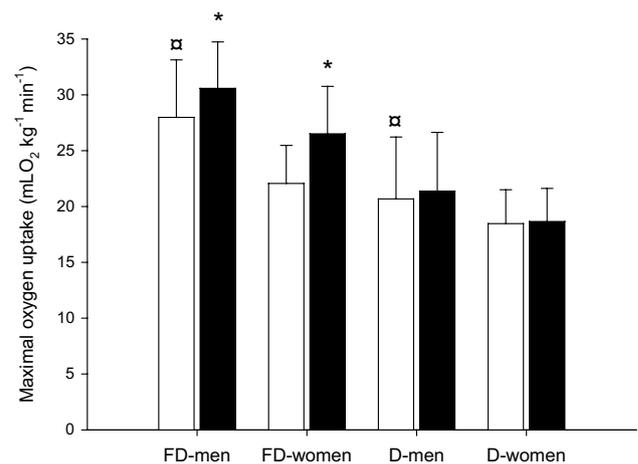
Fig. 5 Maximal oxygen uptake. Maximal oxygen uptake before (open bars) and after (closed) bars the intervention in FD-men, FD-women, D-men and D-women. *($P < 0.05$) different from before the intervention. $^¤$Significantly ($P < 0.05$) different from gender counterparts at baseline

lifestyle-related diseases in men and women (see Krustrup et al. 2010a, b, 2018), as well as with recent meta-analysis reviews (Oja et al. 2015; Milanovic et al. 2015, 2018). However, the present study is the first to evaluate the gender-dependent impact of football training in a group with multiple health challenges by applying a mixed-gender training approach. The men had slightly higher aerobic fitness compared to the women prior to the intervention. However, the cardiovascular loading during training demonstrated a comparable heart rate response between the

genders, which was at a similar high level to that previously observed in various other participant groups (Randers et al. 2010). Indeed, the cardiovascular loading during training is in accordance with findings by Randers et al. (2010) in 30- to 40-year old untrained men and women during 7v7 small-sided games, which can be compared to the type of training performed in the present study. However, in the study by Randers et al. (2010), more high intensity running was performed by the men than the women during the small-sided game training, which may be explained by their younger age and markedly higher

training status. In addition, a greater utilisation of muscle glycogen was observed in the male participant group compared to women, which was reduced by 28 and 11%, respectively. However, as indicated by our findings, age-matched patient groups, such as individuals with prediabetes with comparable a health and fitness level, can perform football training in mixed-gender settings, with women having similar physical loading to men. It should be mentioned that the maximal heart rate values used to calculate the training intensity in the present study were determined during the exhaustive bike test, which may have slightly over-estimated the intensity during the football training.

In our participants, peak oxygen uptake was elevated by 11 and 21% in the male and female football training groups, respectively, with greater relative improvement in the women compared to the men. The increase in peak oxygen uptake between the football groups and the diet groups was also apparent after correcting for the decrease in body mass, while the difference between women and men in the football group vanished (data not shown). The relative increase is more or less in line with other findings (Milanovic et al. 2015). For example, a systematic review and meta-analysis reported that healthy untrained men improved their maximal oxygen uptake by 8–13%, while untrained elderly participants improved their VO_{2max} by 15–18% (Milanovic et al. 2015). Significant improvements in VO_{2max} have also been observed in patients with diabetes mellitus and hypertension (de Sousa et al. 2014; Krustrup et al. 2013; Andersen et al. 2014), whereas minor effects were observed in men with prostate cancer undergoing antiandrogen treatment (Uth et al. 2013, 2014; Schmidt et al. 2017). This puts the men in the present study, with an increase of 11%, in the lower range compared to the literature. Football training for 12–70 weeks in healthy women has previously been shown to increase VO_{2max} by 5–16% (Milanovic et al. 2015), which is less than the current 21% improvement demonstrated in the women with prediabetes. This may be partly due to the low starting levels (22 mL kg^{-1} min^{-1}) of the women in the present study, combined with a potential positive effect of training in a mixed-gender group and receiving dietary advice. In the aforementioned meta-analysis based on seventeen studies, mean improvement in maximal oxygen uptake was 3.51 mL kg^{-1} min^{-1} over a football training intervention, which corresponds well with the findings in our group of elderly subjects with prediabetes. The increase in peak oxygen uptake is supported by a reduction of 4–5 bpm in resting heart rate in both genders, which confirms meta-analysis findings (ES = 6.03 beats min^{-1}; 95% CI 4.43–7.64 (Milanovic et al. 2018), as well as similar increases in VO_{2peak} after correcting for body mass changes. Since the cardiac training responses were equal between men and women, this may have stimulated comparable adaptations in cardiac function in the two genders.

The participants in the present study suffered from mild to moderate hypertension prior to the study, which is a common finding in patients with poor glycaemic regulation or metabolic syndrome (Flores-Le Roux et al. 2011). Mean arterial pressure at baseline was higher in the men (105 mmHg) than in the women (97 mmHg). However, both groups had a reduction of approximately 11 and 7 mmHg in systolic and diastolic blood pressure, respectively, after the intervention. The magnitude of decline is in full agreement with findings in individuals with mild hypertension presented in a recent meta-analysis review by Milanovic et al. (2018) based on seventeen RCTs. This meta-analysis reported higher effect sizes for the improvement in systolic blood pressure in women than in men, and the opposite pattern was apparent for diastolic blood pressure (Milanovic et al. 2018), which indicates some gender differences. However, in the present study we observed similar responses in both genders, which may be linked to our research design involving dietary advice combined with football treatment. Indeed, the women receiving dietary advice alone demonstrated a similar drop in arterial blood pressure to the two football groups, while no change was observed in the men receiving dietary advice alone. Thus, women may be more responsive to dietary advice than men, which may have had an impact on the results of the present study. In addition, diet appears to be highly important for blood pressure control in women.

Blood lipid profile is a strong marker of cardiovascular and metabolic health profile (McQueen et al. 2008). In the present study, total plasma cholesterol was lowered in women only. The women demonstrated a reduction of 0.7 mmol L^{-1}, which is greater than that observed in a meta-analysis of the impact of recreational football on total plasma cholesterol (ES = 0.13 mmol L^{-1}; 95% CI − 0.03 to 0.29 (Milanovic et al. 2018). Plasma LDL cholesterol was reduced in both men and women undertaking football training (− 0.2 and − 0.5 mmol L^{-1}, respectively), which is comparable to other studies (Milanovic et al. 2018). There were no between- or within-group differences for plasma HDL cholesterol or triglyceride, which is in contrast to other observations (Milanovic et al. 2018).

In the present study, resting blood glucose was lowered after the intervention in all four groups, showing that the dietary treatment appears to be the main contributor to a beneficial effect on glycaemic control in the fasting state for elderly men and women with prediabetes. Moreover, football training per se does not provide and additional stimulus to the improved glycemic control. This is in contrast with previous meta-analysis findings suggesting likely trivial effects for blood glucose (ES = 0.00 mmol L^{-1}; 95% CI − 0.22 to 0.22) and possibly trivial effects for glucose tolerance (ES = − 0.13 mmol L^{-1}; 95% CI − 0.49 to 0.22) after periods of football training in untrained subjects (Milanovic

et al. 2018). Notably, resting blood glucose concentrations in all intervention groups approached the clinical threshold of impaired blood glucose control in the present study. However, the absolute blood glucose values were lower at the 120-min time point during OGTT after the intervention in FD-men and FD-women compared to their gender-specific counterparts. As such, the football groups, in contrast to the diet groups, were able to bring the blood glucose concentration closer to baseline values at the end of OGTT, which indicates a positive impact of the football training alone. This points to a decreased risk of diabetes progression (de Sousa et al. 2017), which may indicate that an intervention of football training combined with dietary advice is a more potent treatment strategy for improving glucose tolerance and normalising blood glucose levels than dietary advice alone, which is supported by de Sousa et al. (2014).

In the present study, women obtained similar beneficial adaptations in glycaemic control to men following the intervention and, thus, the potential gender differences in adaptation to T2DM management demonstrated by others (Gouni-Berthold et al. 2008) may in fact be markedly reduced in terms of alterations in glycaemic control when a complex and broad-spectrum training approach is applied. It is generally believed that treatment strategies should be improved in both genders, but women with diabetes may be in need of more aggressive treatment approaches (Kautzky-Willer et al. 2010). In respect of implementing exercise training interventions, men and women with T2DM are reluctant to take up regular exercise regardless of the known therapeutic effects (Danahue et al. 2006), and dropout rates are especially high when participants are left to exercise on their own (Williams et al. 2007). Primary perceived barriers to physical activity among people with T2DM include lack of time and low self-efficacy in the ability to implement exercise. On the other hand, motivators for physical activity include enjoyment of exercise, physical health benefits and social interaction (Jepson et al. 2012; Lidegaard et al. 2016). It is a remarkable finding that untrained recreational football participants report lower perceived exertion during exercise compared to joggers and interval runners, despite the frequently occurring intense actions and periods of high metabolic loading, as indicated by significantly elevated blood lactate levels during training (Randers et al. 2010; Krustrup et al. 2010a). Also, high levels of flow and similar or even less experience of worry during football exercise compared to other traditional exercise modalities, such as running or strength training, have been reported (Elbe et al. 2010). This may be linked to football participants being more focused on psychosocial factors such as enjoyment and the team interaction and dynamics (Ottesen et al. 2010). As such, recreational football may provide a non-conventional, joyful and health-beneficial group-based training method for both genders, which offers a unique and time-efficient strategy

for increasing adherence and life-long exercise continuation in subjects with metabolic disorders (Nielsen et al. 2014).

Obesity and, especially, abdominal fat accumulation are independent risk factors for insulin resistance and T2DM and also detrimental to cardiovascular health (Pedersen and Saltin 2015). In relation to body weight, all treatment groups displayed an intervention-induced decrease, indicating the impact of diet change on weight loss. However, the men and women in the football intervention had a total fat loss of 2.8 and 4.0 kg, respectively, which was greater compared to their gender-specific counterparts (D-men − 1.3 kg and D-women − 1.1 kg) solely following the dietary intervention. Indeed, the body fat loss lowered total body fat percentage from 28 to 25% and 43 to 39% in the football men and women, respectively, with no significant alterations in in the diet groups. In support of this, waist circumference was reduced by 4–5 cm in FD-men and FD-women, respectively, with no change in the D groups. The effect of football training on reducing body fat content is well documented in a new meta-analysis (Milanovic et al. 2018), and cross-sectional studies in elderly football players also show markedly lower body fat content than age-matched sedentary controls (Randers et al. 2014). Overall, football training appears to be a potent manipulator of body fat content in both men and women.

Lean body mass was increased after the intervention in FD-men and FD-women by 0.6 and 0.7 kg, respectively, which was more than in the D groups, which is relevant since T2DM is associated with a decline in muscle mass (Pedersen and Saltin 2015). The higher muscle mass provides a larger total muscle glycogen storage capacity, which is likely to improve clearance of glucose from the bloodstream. This may be of particular importance with advancing age, as the aging process additionally induces changes in body composition, such as increased visceral fat and reduced muscle mass, a concept commonly known as sarcopenic obesity (Baumgartner 2000). Given the progressive loss of muscle mass and strength that accompanies ageing, and the fact that older women appear to become less anabolically sensitive than their older male counterparts (Smith et al. 2008), women may be at increased risk of falls, metabolic disease and decreased quality of life in late adulthood compared to men. As such, it appears of utmost importance for both genders to engage in exercise training routines such as football that offer broad-spectrum health benefits, including muscle mass gains.

Several interesting findings were revealed in relation to bone health. For example, femur neck and shaft BMD were increased by 2–4% in the male and female football groups. Moreover, BMD was elevated at sites in the lower spine. Thus, football training improved bone health at clinically important sites in the proximal part of the femur and lower back in both genders. Moreover, in conjunction with the elevated osteogenic impact of the football training on legs and

spine, the football intervention induced a marked increase in plasma bone turnover markers in men and women, representing increased osteogenesis, remodelling and reabsorption. These findings confirm the findings of several of our previous studies in sedentary young men (Krustrup et al. 2009) and women (Helge et al. 2010), middle-aged men (Andersen et al. 2014) and women (Mohr et al. 2015), elderly subjects (Helge et al. 2014a, b) and other patient groups (Mohr et al. 2014; Uth et al. 2018). Women and men aged 55–70 years with prediabetes, therefore, show a similar osteogenic adaptation to football training.

In conclusion, football training combined with dietary advice causes broad-spectrum health effects in 55- to 70-year-old men and women with prediabetes. The effects of the football treatment only showed minor gender dependency, emphasising that the training-induced effects of football are also marked and clinically relevant for elderly women with prediabetes.

Compliance with ethical standards

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