Soccer Training Improves Cardiac Function in Men with Type 2 Diabetes

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ABSTRACT

SCHMIDT, J. F., T. R. ANDERSEN, J. HORTON, J. BRIX, L. TARNOW, P. KRUSTRUP, L. J. ANDERSEN, J. BANGSBO, and P. R. HANSEN. Soccer Training Improves Cardiac Function in Men with Type 2 Diabetes. *Med. Sci. Sports Exerc.*, Vol. 45, No. 12, pp. 2223–2233, 2013. **Introduction**: Patients with type 2 diabetes mellitus (T2DM) have an increased risk of cardiovascular disease, which is worsened by physical inactivity. Subclinical myocardial dysfunction is associated with increased risk of heart failure and impaired prognosis in T2DM; however, it is not clear if exercise training can counteract the early signs of diabetic heart disease. **Purpose**: This study aimed to evaluate the effects of soccer training on cardiac function, exercise capacity, and blood pressure in middle-age men with T2DM. **Methods**: Twenty-one men age 49.8 ± 1.7 yr with T2DM and no history of cardiovascular disease participated in a soccer training group ($n = 12$) that trained 1 h twice a week or a control group ($n = 9$) with no change in lifestyle. Examinations included comprehensive transthoracic echocardiography, measurements of blood pressure, maximal oxygen consumption ($\dot{V}O_{2max}$), and intermittent endurance capacity before and after 12 and 24 wk. Two-way repeated-measures ANOVA was applied. **Results**: After 24 wk of soccer training, left ventricular (LV) end-diastolic diameter and volume were increased ($P < 0.001$) compared to baseline. LV longitudinal systolic displacement was augmented by 23% ($P < 0.001$) and global longitudinal two-dimensional strain increased by 10% ($P < 0.05$). LV diastolic function, determined by mitral inflow (E/A ratio) and peak diastolic velocity E', was increased by 18% ($P < 0.01$) and 29% ($P < 0.001$), respectively, whereas LV filling pressure E/E' was reduced by 15% ($P = 0.05$). Systolic, diastolic, and mean arterial pressures were all reduced by 8 mm Hg ($P < 0.01$, $P < 0.001$, and $P < 0.001$, respectively). $\dot{V}O_{2max}$ and intermittent endurance capacity was 12% and 42% ($P < 0.001$) higher, respectively. No changes in any of the measured parameters were observed in control group. **Conclusion**: Regular soccer training improves cardiac function, increases exercise capacity, and lowers blood pressure in men with T2DM. **Key Words:** ECHOCARDIOGRAPHY, TISSUE DOPPLER IMAGING, BLOOD PRESSURE, FOOTBALL, HIGH-INTENSITY TRAINING

The type 2 diabetes mellitus (T2DM) pandemic is estimated to affect nearly 500 million people by the year 2030, and T2DM is associated with a two- to fourfold risk of dying from heart disease (10,35). Besides macrovascular complications such as coronary artery disease, T2DM is independently associated with heart failure, and diastolic left ventricular (LV) dysfunction has been described as the first marker of diabetic heart disease, with a prevalence as high as 70% in patients with preserved LV ejection fraction (12,13). However, the development of novel features in modern echocardiography, such as tissue Doppler imaging (TDI) and speckle tracking two-dimensional (2-D) strain analysis, has challenged the view that diastolic dysfunction is the first marker of diabetic heart disease (13,15). Indeed, echocardiographic strain analysis may detect subclinical signs of systolic dysfunction in 25% of T2DM patients with normal LV diastolic function and ejection fraction (EF) (13).

Physical activity is a cornerstone for the nonpharmacological treatment of T2DM aimed at enhanced overall health status, for example, with improved glycemic and blood pressure (BP) control, increased exercise capacity, and reduction of overall mortality (1,28). Furthermore, physical activity has been suggested to improve cardiac function, but the reported effects of exercise on cardiac function in T2DM patients are conflicting (9,21,27). These diverging results may relate to differences in the training interventions (organization, duration, intensity, adherence, etc.), T2DM duration, and/or other system- or patient-related factors. Also, in patients

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with heart failure, improvements of cardiac function are more pronounced with high-intensity interval training than with continuous moderate training (40). Moreover, in patients with T2DM, the greatest improvement of exercise capacity appears to be more related to exercise intensity than to exercise volume (8). Interestingly, the effect on cardiac function of a high-intensity exercise modality in T2DM patients has not to our knowledge been investigated.

Despite a large body of evidence on the cardiovascular benefits of exercise training, less than 50% of the European population is involved in aerobic leisure time activities, and the development of strategies for subjects to increase physical activity and hereafter to maintain a physically active lifestyle is warranted, especially in T2DM patients (31). Soccer is a universally popular team sport, and recent evidence from our group has suggested that soccer training may improve cardiac function, augment exercise capacity, and reduce BP in men with hypertension and sedentary women (4,23,25). Soccer training is comparable with high-intensity interval training and involves psychological and social interactions that raise the social capital of participants and motivate for adherence with the intervention and a long-term physically active lifestyle (30). The aim of the present study therefore was to evaluate the effects of a 24-wk soccer training intervention in physically inactive men with T2DM on myocardial function evaluated by comprehensive echocardiography, along with exercise capacity, BP, and peripheral arterial tonometry variables, respectively.

METHODS

Subjects. From the start of October 2011 to the mid of January 2012, a total of 121 sedentary men age 35–60 yr with T2DM, registered in the outpatient clinical database of Steno Diabetes Centre, a dedicated diabetes clinic and research institution, were contacted by postal mail or telephone (Fig. 1). Inclusion criteria were diagnosis of type 2 diabetes and stable long-term glycosylated hemoglobin (HbA1C) levels for at least 3 months. Exclusion criteria were history or symptoms of cardiovascular disease or

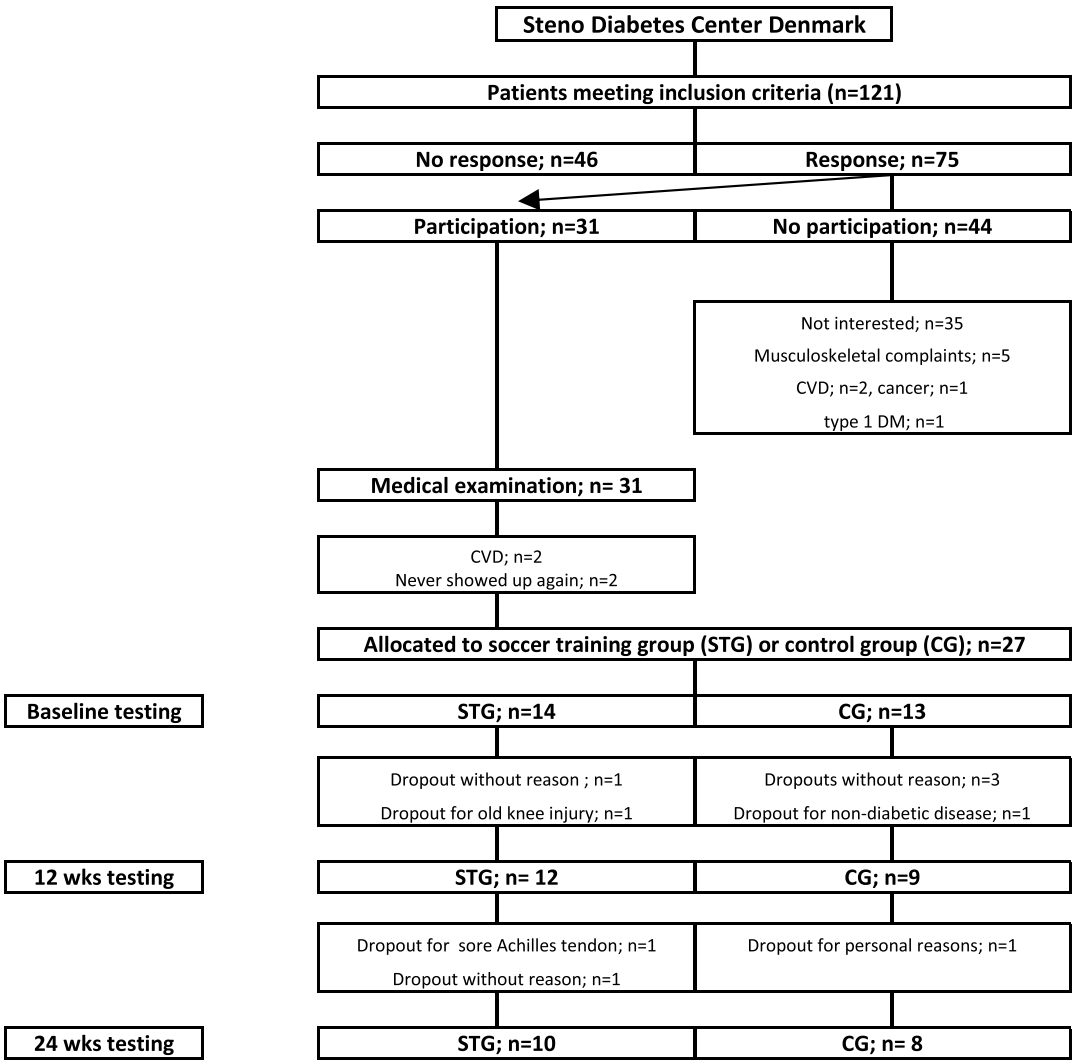

FIGURE 1—Figure 1 shows the recruitment process of patients with T2DM from Steno Diabetes Center, Denmark. CVD; cardiovascular disease.

cancer, diabetic complications (nephropathy [plasma creatinine > 90 μmol·L^{-1}], retinopathy and neuropathy), type 1 diabetes mellitus, treatment with beta-blockers (due to their heart rate-lowering properties), or musculoskeletal complaints that were considered to preclude soccer training. Seventy-five patients (62%) responded, of which 35 were not interested in participation in the study, mainly for practical reasons (long travelling distances to the soccer training or study testing sites, busy work schedules, etc.), and 9 subjects were excluded because of cardiovascular disease (n = 2), cancer (n = 1), type 1 diabetes mellitus (n = 1), or musculoskeletal complaints (n = 5). The remaining 31 patients underwent screening with medical examination, 12-lead ECG, and echocardiography (see following sections). No structural or valvular heart disease was found at the study screening echocardiography, but two subjects were subsequently excluded for undiagnosed coronary artery disease and sick sinus syndrome, respectively, and referred to their local hospital. Two subjects never showed up for scheduled testing after the medical examination. In total, of the 75 responding subjects, 27 (36%) were therefore eligible for enrolment in the study and accepted to participate. However, before the start of the intervention, 4 wk after patient accept, four subjects dropped out due to heavy workload, family priorities, psychological reasons, or concerns over a previous knee injury, respectively.

Design. We aimed to conduct a randomized study, but early in the recruitment process, it became apparent that randomization was not feasible, primarily because several subjects denied randomization and requested allocation to soccer training (n = 7) or no training (n = 9). Individual preferences for no training were determined by practical issues including long travelling distance to the training facilities and/or busy work schedules. However, after this selection process, subjects were found to be comparable in age, diabetes duration, body mass index (BMI), and $\dot{V}O_{2max}$ between the two groups (Table 1).

The study hence included 21 subjects, of which 12 participated in the soccer training group (STG), where they trained twice a week for 60 min as a supplement to their routine treatment and habitual daily physical activity, or the control group (CG, n = 9), where subjects were instructed to maintain their daily physical activity level and not to change their lifestyle during the study period. In STG, 12 (100%) and 10 (83%) of the subjects completed the soccer training intervention from 0 to 12 wk and from 0 to 24 wk, respectively. In CG, 9 (100%) and 8 (89%) of the subjects completed the protocol investigations after 12 and 24 wk, respectively. All subjects were informed verbally and in writing about any potential discomforts or risks related to the experimental study protocol and signed informed written consent. The study was conducted according to the Declaration of Helsinki and was approved by the local ethical committee of Copenhagen (H-2-2011-088). The study was reported at ClinicalTrials.gov (identifier: NCT01636349).

Soccer training intervention. Soccer training was performed twice a week for 1 h for a 24-wk period. The training was organized indoor on a 20-m wide × 40-m long wooden court surrounded by walls. Sessions consisted of ordinary four-a-side, five-a-side, and six-a-side matches as used in a series of previous studies (23–25). The subjects played five 10-min game periods interspersed by 2 min of passive rest periods.

Heart rate was recorded in 1-s intervals with chest belts (Polar Team System; Polar Oy, Kempele, Finland). HR_{max} was determined as the highest obtained heart rate observed

TABLE 1. Characteristics of subjects completing 12 wk of training: age (yr), height (cm), weight (kg), BMI (kg·m^{-2}), systolic BP (mm Hg), diastolic BP (mm Hg), RHR (bpm), glycosylated hemoglobin (HbA1c; %), maximal oxygen consumption ($\dot{V}O_{2max}$; mL·min^{-1}·kg^{-1}), total cholesterol (mmol·L^{-1}), low-density lipoprotein cholesterol (LDL; mmol·L^{-1}), high-density lipoprotein cholesterol (HDL; mmol·L^{-1}), triglycerides (mmol·L^{-1}), duration of diabetes (yr), and medication in men with T2DM before and after 12 and 24 wk of soccer training (n = 12) and controls (n = 9) with no change in lifestyle.

	STG			CG			ANOVA P	
	Baseline	12 wk	24 wk	Baseline	12 wk	24 wk	Time	Time × Group
Age (yr)	50.6 ± 7.1	50.8 ± 7.1	51.0 ± 7.1	48.7 ± 9.2	48.9 ± 9.2	49.1 ± 9.2		
Height (cm)	176.8 ± 6.8	176.8 ± 6.8	176.8 ± 6.8	182.2 ± 6.6	182.2 ± 6.6	182.2 ± 6.6		
Weight (kg)	95.4 ± 14.8	94.6 ± 14.7	94.3 ± 14.6	100.4 ± 18.4	101.0 ± 18.5	101.0 ± 19.8	0.86	0.05
BMI (kg·m^{-2})	30.4 ± 3.4	30.1 ± 3.3	30.0 ± 3.4	30.4 ± 6.7	30.6 ± 6.8	30.7 ± 7.3	0.93	0.05
Systolic BP (mm Hg)	138 ± 15	129 ± 12***	129 ± 16***	126 ± 14	131 ± 18	129 ± 18	0.31	<0.001
Diastolic BP (mm Hg)	89 ± 7	82 ± 7***	81 ± 7***	84 ± 8	85 ± 10	84 ± 11	<0.01	<0.001
RHR (bpm)	68 ± 10	63 ± 7	62 ± 6	68 ± 16	69 ± 19	70 ± 21	0.30	0.06
HbA1c (%)	7.4 ± 1.2	6.9 ± 1.2**	7.0 ± 1.1**	7.5 ± 1.2	7.4 ± 1.2	7.5 ± 1.2	<0.01	0.21
$\dot{V}O_{2max}$ (mL·min^{-1}· kg^{-1})	30.5 ± 2.9	34.0 ± 2.5***,††	34.1 ± 3.3***,††	27.5 ± 8.2	27.5 ± 9.8	28.0 ± 7.4	<0.001	<0.01
Total cholesterol (mmol·L^{-1})	4.4 ± 0.9	4.6 ± 1.0	4.2 ± 0.9	3.9 ± 0.9	4.1 ± 1.1	4.2 ± 1.3	0.56	0.21
LDL-C (mmol·L^{-1})	2.7 ± 0.9	2.7 ± 0.8	2.4 ± 0.8	2.3 ± 0.9	2.4 ± 1.0	2.5 ± 1.0	0.24	0.60
HDL-C (mmol·L^{-1})	1.2 ± 0.2	1.2 ± 0.2	1.3 ± 0.3	1.1 ± 0.3	1.2 ± 0.4	1.2 ± 0.3	0.82	0.24
Triglycerides (mmol·L^{-1})	1.3 ± 0.5	1.5 ± 0.7	1.6 ± 0.8	1.2 ± 0.4	1.2 ± 0.4	1.5 ± 0.8	0.20	0.67
Duration of diabetes (yr)	7.1 ± 2.2			7.5 ± 3.6				
Medication, n (%)							Fischer's exact test P values	
Oral antidiabetic drugs	11/12 (92%)	11/12 (92%)	9/10 (90%)	6/9 (67%)	6/9 (67%)	5/8 (63%)		0.27
Insulin	2/12 (17%)	2/12 (17%)	2/10 (20%)	3/9 (33%)	3/9 (33%)	3/8 (38%)		0.61
Antihypertensive drugs	7/12 (58%)	7/12 (58%)	7/10 (70%)	6/9 (67%)	6/9 (67%)	5/8 (63%)		1.00
Statins	6/12 (50%)	6/12 (50%)	6/10 (60%	6/9 (67%)	6/9 (67%)	5/8 (63%)		0.66
Aspirin	9/12(75%)	9/12(75%)	7/10 (70%)	6/9 (67%)	6/9 (67%)	5/8 (63%)		1.00

Values are presented as mean ± SD. Right column presents the ANOVA P values from time effect and time × group effect (interaction).
***P < 0.001, **P < 0.01, *P < 0.05 different from baseline; †††P < 0.001, ††P < 0.01, †P < 0.05 different from CG.

in 10-s intervals at any training session or test (HR_{max}; 177 ± 8 bpm). Data were later transferred to a computer using Polar Team2 software (Polar Team System). The total number of training sessions was, on average, 29.6 (1.20 [range 0.7–1.7] per week), corresponding to a training attendance of 60% for each subject. Training intensity analysis revealed that 43% ± 22% of the total training time was spent higher than 85% of HR_{max} (151 ± 7 bpm), and the average intensity for all training performed was 82% ± 6% of HR_{max} (145 ± 10 bpm.).

Habitual physical activity level. To estimate the daily physical activity level of all participants outside the soccer training sessions, stride counts were measured using Yamaxx pedometers (Yamaxx Digi-Walker, model SW 701; Yamasa Tokei Keiki Co., Ltd., Tokyo, Japan). Subjects were instructed to wear pedometers for a 3-d period, including 1-d during the weekend. In addition, stride counts were multiplied by each individual's obtained walking stride length to yield movement distance in meters. Also, to monitor quality of movement as well as any changes in daily physical activity levels over the course of the study, the participants were asked to fill out a modified Danish version of the Physical Activity Scale (PAS) 2 questionnaire (3). All pedometer and PAS 2 data were then converted into daily scores (strides per day, meters per day, or minutes per day, respectively). No differences in daily physical activity levels were detected between STG and CG as measured by pedometer stride counts (4444 ± 824 vs 5579 ± 868 strides per day; NS) or walking distance (3656 ± 686 vs 4869 ± 911 $m \cdot d^{-1}$, NS). Also, self-reported participation in moderate to strenuous PAS 2 questionnaire categories was not different between the two groups before the study (338 ± 71 vs 250 ± 83 $min \cdot wk^{-1}$; NS), and all subjects therefore at baseline and throughout the study fulfilled the guideline-recommended 30-$min \cdot d^{-1}$ physical activity (this being representative of the "routine treatment") (2). During the study, no changes in habitual physical activity levels were reported by any subjects in STG besides participation in soccer training. In CG, all subjects also did not change their habitual physical activity level during the study.

Medication. All subjects were asked to maintain their prescribed medication, for example, glucose-lowering agents, antihypertensive drugs (except for beta-blockers), and statins, throughout the study and to report any changes herein during the study period (Table 1). During the study period, one subject in STG was reduced in oral antidiabetic medication dose because of very low HbA1C values, and one subject reduced his daily insulin intake by 10%. In addition, in CG, one subject was changed from one long-acting insulin agent to another due to unstable blood glucose levels.

Echocardiography. Comprehensive transthoracic echocardiography was performed on a GE Vivid 9 ultrasound machine with a 2.5-MHz transducer (GE Healthcare, Horton, Norway) before the study and after 12 and 24 wk. The examination was performed with the subjects resting in lateral supine position in a dark room by three experienced echocardiographers. All examinations were analyzed offline in random order, using the Echo Pac software version BT 11.0. One-third of all examinations were reanalyzed by an independent and blinded echocardiographers, and no significant interobserver variation in measurements was found (data not shown). Cardiac structure was evaluated from parasternal long axis 2-D recordings at the mid-ventricular level, with measurement of LV end-diastolic diameter, interventricular septal wall thickness (IVST), and posterior wall thickness (PWT). LV mass was calculated from the formula 0.832 [1.05 [$(LVID + IVST + PWT)^3$] − $(LVID)^3$] and indexed according to body surface area, and LV volumes and EF (%) were evaluated with Simpson's biplane method. Right ventricular function was evaluated as tricuspid annular plane systolic excursion (TAPSE), with the curser placed in the lateral annulus of the tricuspid valve using M-mode in the apical four-chamber view. TAPSE was calculated as the total tricuspid annular longitudinal displacement (cm) from end diastole to end systole. Peak transmitral inflow velocity measures in early (E) and late (A) diastole and the corresponding E/A ratio was measured using pulsed Doppler in the apical four-chamber view with the curser between the tips of the mitral leaflets. Pulsed analyses of TDI measurements of diastolic velocities are less load dependent than transmitral flow measurements with pulsed Doppler (20) and were obtained with a 5-mm pulsed (TDI) sample volume placed in the lateral, septal, anterior, and inferior plane of the mitral annulus in the two- and four-chamber apical views and included peak systolic velocity (S'; $cm \cdot s^{-1}$), peak early diastolic velocity (E'; $cm \cdot s^{-1}$), and peak late diastolic velocity (A'; $cm \cdot s^{-1}$). The values of E' represented the average of the septal and lateral early peak diastolic velocities, and E/E' was calculated as a measure of LV filling pressure. Two-dimensional color tissue Doppler ($_{TDIcolor}$) at a frame rate >$120 \cdot s^{-1}$ was evaluated from six basal segments of septal, lateral, anterior, inferior, posterior, and anterior lateral walls of the apical two- and four-chamber views, long axis, and values were averaged. Measurements included peak systolic velocity color S' ($S'_{TDIcolor}$), peak early diastolic velocity color E' ($E'_{TDIcolor}$), and peak late diastolic velocity color A' ($A'_{TDIcolor}$). Diastolic dysfunction was defined from abnormal mitral inflow patterns ($E < A$), and pseudo-normalization was excluded when $E > A$ and $E' \geq 8$ $cm \cdot s^{-1}$, as previously suggested (20). Furthermore, diastolic dysfunction with or without presence of increased LV filling pressure was defined as ($E/E' \geq 15$). LV longitudinal systolic function was also evaluated by speckle tracking analysis. Longitudinal 2-D global strain was estimated using automated functional imaging. In brief, we obtained the LV global longitudinal strain (GS) from the movements of speckles ("kernels" or acoustic markers) in grayscale 2-D images with a frame rate of 50–80 Hz. From the geometric shift of these speckles, the contraction and relaxation of the myocardium can be measured, and GS was expressed as the average of the maximal systolic displacement in each basal segment determined in the six standard apical projections (34). LV longitudinal systolic shortening (LV

displacement) was evaluated using tissue tracking as described previously (36).

BP and resting heart rate. BP was measured before the study, as well as after 12 and 24 wk of the study period. No physical activity or training was performed in the 2 d before these measurements, which were performed in a quiet dark room under standardized conditions after an overnight fast. Measurements of systolic BP, diastolic BP, and mean arterial pressure (MAP; diastolic BP + 1/3 [systolic BP − diastolic BP]) were performed between 8:00 and 9:00 a.m. to avoid diurnal variations. The subjects rested for at least 15 min in supine position, and BP was measured five to seven times by an automated BP monitor (M7; OMRON, Vernon Hills, IL) on the left upper arm. Resting heart rate (RHR) was determined as the lowest average value obtained by the monitor during a 1-min period.

Maximal oxygen uptake. After 0, 12, and 24 wk of the intervention period, $\dot{V}O_{2max}$ ($mL \cdot min^{-1} \cdot kg^{-1}$) (OxyconPro; VIASYS Healthcare, Hoechberg, Germany) and HR_{max} (Polar Team System; Polar Electro Oy, Kempele, Finland) were measured during a standardized cycling protocol performed on an electronically braked ergometer bike (Monark E839). Subjects started to exercise at a work pace and workload of 80 rpm and 40 W, respectively, and the workload was increased by 20 W every 2 min until volitional fatigue. $\dot{V}O_{2max}$ was determined as the highest value achieved during a 30-s period, and HR_{max} was determined as the highest value achieved throughout the test.

Intermittent endurance capacity. Before the intervention period and after 12 wk, intermittent endurance capacity was measured using the Yo-Yo Intermittent Endurance test Level 1 (Yo-Yo IE1) as previously described (24). The Yo-Yo IE1 test consisted of 2 × 20-m shuttle runs performed at increasing running speeds, interspersed with 5 s of active recovery during which the participants jogged around a cone placed 2.5 m behind the start/finishing line. The speeds were controlled by audio signals from a CD. The Yo-Yo IE1 test was performed indoor on a wooden floor after a standardized 10-min low-intensity warm-up procedure. The test was terminated when the subject was no longer able to maintain the required speed. The total distance (meters) covered represented the test result for each individual.

Body composition and blood samples. At baseline and after 12 and 24 wk, a whole-body DXA scan (Prodigy Advance; Lunar Corporation, Madison, WI) was performed between 7:00 and 9:00 a.m. under standardized conditions after an overnight fast. The effective radiation dose was 0.6 mSv per scan. Height (cm) and total body weight (kg) were also recorded, and BMI ($kg \cdot m^{-2}$) was calculated using the Encore 2006 software (Lunar Corporation). Blood samples were obtained from a cubital vein between 7:00 and 10:00 a.m. under standardized conditions after an overnight fast. All blood samples were analyzed for total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and glycosylated hemoglobin (HbA1c), respectively, by automated analyzers (Cobas Fara; Roche, Neuilly sur Seine, France) using enzymatic kits (Roche Diagnostics, Mannheim, Germany; and Tosoh G7, Tosoh Europe, Tessenderlo, Belgium) in the clinical laboratory at Rigshospitalet, Copenhagen, Denmark. Detailed body composition data, and results of the metabolic and other investigations, will be reported elsewhere.

Peripheral vascular function. Peripheral arterial tonometry (PAT) measurements of the reactive hyperemic index and the augmentation index, respectively, were measured before the study, as well as after 12 and 24 wk of the study period. PAT was performed under standardized conditions in a quiet dark room between 8:00 and 10:00 a.m. The subjects were instructed to avoid intake of medication, caffeine, and vitamins for 12 h before the examination. A pneumatic probe was placed on the tip of each index finger and connected to a plethysmographic device (EndoPat-2000; Itamar Medical Ltd., Caesarea, Israel). After a 15-min resting period, heart rate variability was registered by the device during a 6-min period. Hereafter, PAT measurements were made before and during reactive hyperemia as previously described with provision of the reactive hyperemia index (RHI, a measure of microvascular endothelial function) and augmentation index (a measure of arterial stiffness, normalized to a heart rate of 75 bpm), respectively (11).

Statistics. Before the study, potential parametric group differences were analyzed with a two-tailed unpaired *t*-test and nonparametric variables with Fischer's exact test. Between- and within-group changes after 12 and 24 wk were analyzed with two-way repeated-measures ANOVA. When a significant time–group (interaction) was found, Tukey's honest significance *post hoc* tests were conducted. All ANOVA main effects (time effect and time–group effect) are presented in the right column of Tables 1 and 2. Baseline differences were observed between STG and CG in diastolic values (E/A ratio, E', MV deceleration time, and E/E'). These results were therefore tested with ANCOVA statistics adjusted for baseline values. In addition, the magnitude of changes according to low versus high baseline values was tested in STG using median split. Pearson product placement was used to test associations between selected variables, and McNemar's test was used to test the proportion of subjects with diastolic dysfunction before and after the study. There were three study dropouts from 12 to 24 wk, and for missing values, we used the last observation carried forward method (Fig. 1). All analyses were controlled with two-way repeated-measures ANOVA without imputations, and no relevant statistical differences were found. $P < 0.05$ was used as the level of significance. All data are presented as mean ± SD, unless otherwise indicated. Statistical analyses were performed using Sigma plot, version 11.0.

RESULTS

Cardiac Structure and Function

Cardiac dimensions. LV end-diastolic diameter and LV end-diastolic volume were higher after 12 wk ($P < 0.01$)

and 24 wk ($P < 0.001$) of training in STG (Table 2). In addition, LV mass index in STG was 12% ($P < 0.05$) and 16% ($P < 0.01$), which increased after 12 and 24 wk, respectively. No changes in cardiac dimensions were observed in the CG (Table 2).

Systolic function. All subjects had normal (>55%) LV ejection fraction, and no change herein was observed during the study (Table 2). In STG, LV displacement, that is, LV longitudinal shortening by tissue tracking, was elevated ($P < 0.001$) by 19% and 23% after 12 and 24 wk of training, respectively, with no change in CG (Table 2 and Fig. 2). Furthermore, in STG, GS was increased by 8% and 10% ($P < 0.05$) after 12 and 24 wk of training, respectively, whereas a decrease in GS strain of 7% ($P < 0.05$) and 10% ($P < 0.01$), respectively, was observed in CG (Table 2 and Fig. 2). A 15%–17% ($P < 0.05$) increase in $S'_{TDIcolor}$ was observed only in STG after 12 and 24 wk of training (Table 2). Also, TAPSE was elevated 19% ($P < 0.001$) after 12 and 24 wk of training only in STG (Table 2). A positive correlation ($r = 0.67$, $P < 0.05$) was observed in STG between increased $\dot{V}O_{2max}$ and increased LV end-diastolic volume after 24 wk of training.

Diastolic function. During the study, diastolic function was markedly improved after football training. At baseline, diastolic LV echocardiographic parameters were generally lower in STG compared to the CG, including E/A ratio ($P < 0.05$), mitral valve deceleration time ($P < 0.05$), E/E' ($P < 0.05$), and E' ($P < 0.05$) (Table 2). At baseline, diastolic dysfunction as defined by an abnormal pattern of mitral inflow ($E < A$) was found in 75% and 33% of the subjects in STG and CG, respectively, and the percentage of subjects with diastolic dysfunction was reduced to 50% ($P = 0.25$) after 12 and 24 wk in STG but was unchanged in CG during the study period. Overall, in STG, the E/A ratio was elevated by 11% ($P < 0.05$) and 18% ($P < 0.01$), and mitral valve deceleration time was reduced by 17% ($P < 0.05$) and 13% ($P < 0.05$) after 12 and 24 wk of training, respectively (Table 2 and Fig. 2). In STG, TDI measures of E' were increased after 24 wk of training by 29% ($P < 0.01$) for E' (Table 2 and Fig. 4) and 17% ($P < 0.01$) for $E'_{TDIcolor}$ (Table 2). Furthermore, LV filling pressure as assessed by E/E' was reduced by 15% in STG ($P = 0.05$), and the two subjects in STG with $E/E'>15$ normalized their LV filling pressures after only 12 wk of training. In CG, no significant changes in any diastolic parameters were observed (Table 2). The improvements in diastolic variables including E/A ratio, E', mitral valve deceleration time, and E/E' remained significant ($P < 0.01$, $P < 0.01$, $P < 0.05$, and $P < 0.05$, respectively) when adjusted for baseline values. Furthermore, no differences in the magnitude of changes in the primary diastolic outcome variables were observed in STG when categorized according to high or low baseline values (E/A ratio; low 31% vs high 10%, $P = 0.28$, E'; low 33% vs high 22%, $P = 0.95$), but differences were observed for other variables (mitral valve deceleration time; high −17% vs low +5%, $P < 0.01$ and E/E'; high −21% vs low +2%, $P < 0.05$).

BP and RHR

Systolic BP in STG was reduced by 8 mm Hg after 12 wk ($P < 0.001$) and 24 wk ($P < 0.01$) of training (137 ± 15 vs 129 ± 12 and 129 ± 16 mm Hg; Fig. 3A). In STG, diastolic

TABLE 2. Echocardiographic parameters in men with type 2 diabetes before and after 12 and 24 wk of soccer training ($n = 12$) and controls ($n = 9$) with no change of lifestyle, before and after 12 and 24 wk.

	STG			CG			ANOVA *P*	
	Baseline	12 wk	24 wk	Baseline	12 wk	24 wk	Time	Time × Group
LV Structure								
LV end-diastolic diameter (cm)	5.0 ± 0.1	5.2 ± 0.1**,†††	5.3 ± 0.1***,†††	4.8 ± 4.7	4.7 ± 0.1	4.7 ± 0.1	0.06	<0.01
LV end-diastolic volume (mL)	119.2 ± 6.2	126.7 ± 7.0**	135.0 ± 7.6***,†	120.7 ± 10.1	116.4 ± 12.7	115.5 ± 10.3	<0.05	<0.001
LV mass index ($g \cdot m^{-2}$)	79.0 ± 3.8	88.2 ± 2.7*,†††	91.4 ± 2.8**,†††	70.3 ± 3.4	69.9 ± 4.8	67.1 ± 3.4	0.16	<0.05
Systolic function								
EF biplane (%)	58.1 ± 1.0	59.5 ± 1.2	60.6 ± 0.8	58.1 ± 1.1	59.5 ± 1.5	59.5 ± 1.1	<0.05	0.19
TAPSE (cm)	2.1 ± 0.1	2.5 ± 0.1***,†	2.5 ± 0.1***,†	2.2 ± 0.1	2.2 ± 0.1	2.1 ± 0.1	<0.05	<0.001
S' ($cm \cdot s^{-1}$)	0.08 ± 0.01	0.09 ± 0.01	0.09 ± 0.00	0.08 ± 0.00	0.08 ± 0.00	0.08 ± 0.00	0.16	0.59
$S'_{TDIcolor}$ ($cm \cdot s^{-1}$)	6.1 ± 0.4	7.0 ± 0.7*	6.9 ± 0.5*	6.0 ± 0.4	6.5 ± 0.2	6.4 ± 0.4	<0.05	0.47
GS (%)	−15.5 ± 0.9	−16.8 ± 0.7*	−17.0 ± 0.7*	−17.5 ± 1.0	−16.2 ± 1.1*	−15.7 ± 1.4**	0.88	<0.001
LV displacement (mm)	9.7 ± 0.7	11.5 ± 0.9***	11.9 ± 0.7***	10.6 ± 0.8	11.1 ± 0.8	10.1 ± 0.8	<0.001	<0.001
Diastolic function								
Mitral inflow velocity *E/A* ratio	0.9 ± 0.1	1.0 ± 0.1*	1.1 ± 0.1**,§	1.2 ± 0.1†	1.1 ± 0.1	1.1 ± 0.1	0.75	<0.001
Mitral deceleration time (ms)	214.8 ± 14.7	178.0 ± 8.7*	186.0 ± 7.3*	176.2 ± 8.4†	198.3 ± 14.0	186.4 ± 14.6	0.63	<0.05
E/E'	9.7 ± 1.2	8.5 ± 0.7	8.4 ± 0.7*	6.8 ± 0.5†	7.5 ± 0.6	7.2 ± 0.6	0.57	<0.05
A' ($cm \cdot s^{-1}$)	0.11 ± 0.1	0.11 ± 0.0	0.11 ± 0.1	0.09 ± 0.0	0.10 ± 0.0	0.10 ± 0.1	0.604	0.124
E' ($cm \cdot s^{-1}$)	0.07 ± 0.01	0.09 ± 0.01**	0.09 ± 0.01**	0.10 ± 0.00†	0.10 ± 0.01	0.09 ± 0.01	0.06	<0.05
$E'_{TDIcolor}$ ($cm \cdot s^{-1}$)	6.0 ± 0.7	7.0 ± 0.1***	7.1 ± 0.5***	7.8 ± 0.6†	8.8 ± 0.5	7.9 ± 0.6	<0.01	<0.05

Right column presents the ANOVA *P* values of time effects and time–group effects (interaction). Values are presented as mean ± SD.
***$P < 0.001$, **$P < 0.01$, *$P < 0.05$ different from baseline; †††$P < 0.001$, ††$P < 0.01$, †$P < 0.05$ different from CG; ‡$P < 0.05$ different from STG at baseline; §$P < 0.05$ different from 12 wk.
LV, left ventricular; EF, ejection fraction by Simpson biplane method; TAPSE, tricuspid annular plane systolic excursion. S', E', and A' are values from pulsed wave TDI. $S'_{TDIcolor}$ and $E'_{TDIcolor}$ are values from Color TDI. GS, 2-D speckle tracking global strain. LV displacement values obtained by tissue tracking.

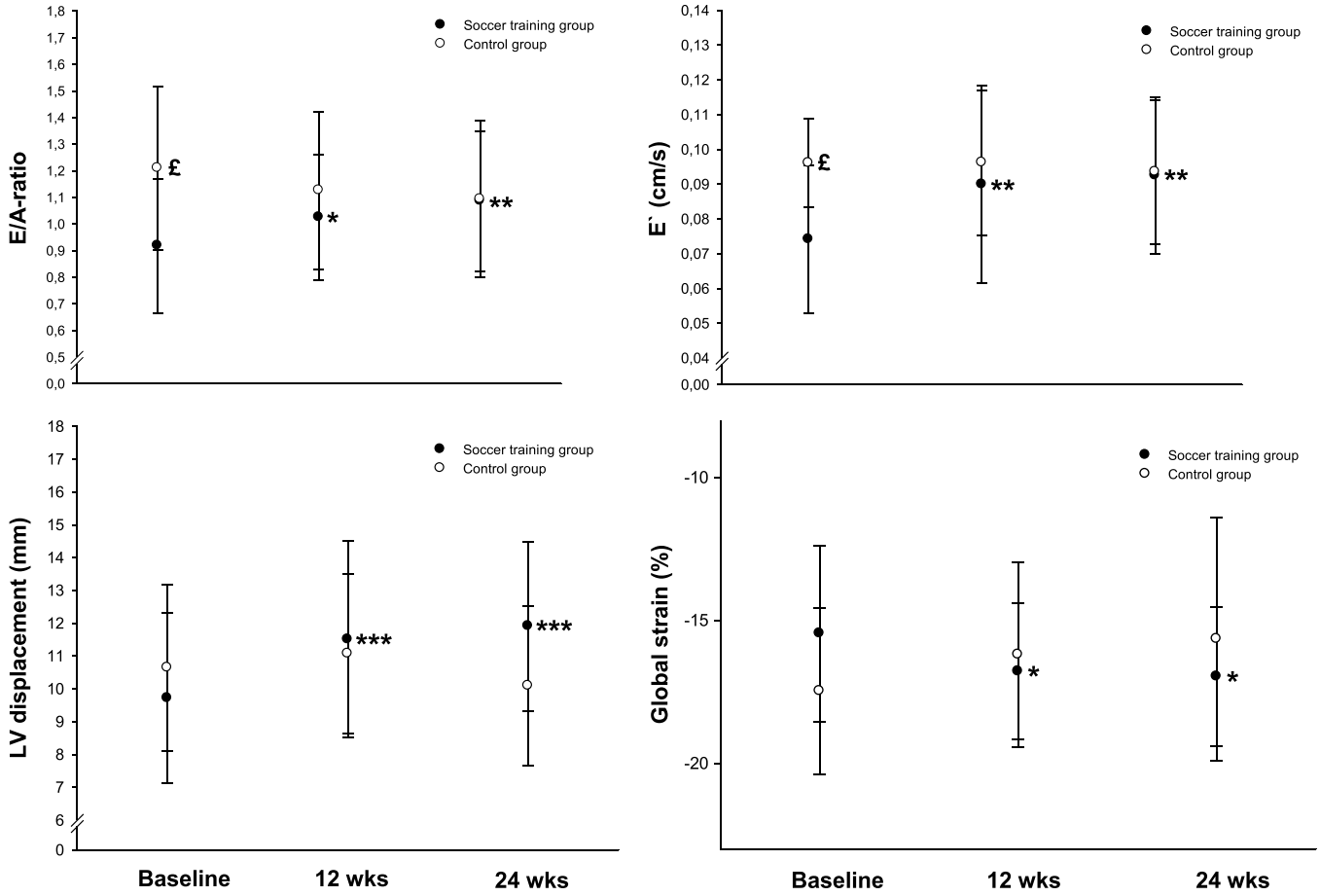

FIGURE 2—Changes in diastolic (*E*/*A* ratio and *E*′) and systolic function (LV displacement and GS) in men with T2DM before and after 12 and 24 wk of soccer training (n = 12) and controls (n = 9) with no change in lifestyle. ***$P < 0.001$, **$P < 0.01$ different from baseline. $^{£}P < 0.05$ different from STG at baseline. Values are mean ± SD.

BP was 7 and 8 mm Hg lower ($P < 0.001$) after 12 and 24 wk of training (89 ± 7 vs 82 ± 7 and 81 ± 7 mm Hg; Fig. 3B), respectively. Consequently, in STG, the MAP reductions were of similar magnitude (Fig. 3C). In CG, no changes in systolic (126 ± 14 vs 131 ± 18 and 129 ± 18 mm Hg) or diastolic (84 ± 8 vs 85 ± 10 and 84 ± 11 mm Hg) BPs were observed (Figs. 3A and 3B). In STG, a tendency ($P = 0.07$) toward a reduced RHR was observed after 24 wk of training (68 ± 10 vs 62 ± 6 bpm), with no change for CG (68 ± 16 vs 70 ± 21 bpm; Table 1). Negative correlations were found between increased $\dot{V}O_{2max}$ and reduced diastolic BP ($r = -0.71$, $P < 0.001$; Fig. 4A) and MAP ($r = -0.68$, $P < 0.05$; Fig. 4B), respectively, after 24 wk of training in STG.

Maximum Oxygen Uptake and Exercise Capacity

$\dot{V}O_{2max}$ in STG was 30.5 ± 2.9 $mL \cdot min^{-1} \cdot kg^{-1}$ before training and was higher ($P < 0.001$) after 12 wk (11%) and 24 wk (12%) of soccer training (Table 1). No changes in $\dot{V}O_{2max}$ were observed in CG (Table 1). After 12 wk of training, intermittent endurance capacity (Yo-Yo IE1) was increased by 42% in STG (893 ± 353 vs 1270 ± 453 m, $P < 0.001$), with no change observed in CG (733 ± 541 vs 785 ± 637 m, NS).

BMI and Blood Samples

In STG, BMI ($P = 0.05$) and HbA1c ($P < 0.01$) were lowered 1% and 5%, respectively, during the study. No changes in these parameters were observed in CG (Table 1). No significant differences at baseline or changes during the study were observed in total cholesterol, LDL-C, HDL-C, and triglyceride levels in STG or CG (Table 1).

Peripheral Vascular Function

At baseline, RHI was not different between STG and CG ($P = 0.6$). In STG, the baseline RHI of 2.00 ± 0.4 was not changed significantly after 12 and 24 wk (1.91 ± 0.5 and 2.03 ± 0.6, respectively). In CG, RHI was 1.93 ± 0.3 at baseline and also did not change after 12 and 24 wk (1.89 ± 0.6 and 1.90 ± 0.4, respectively). No change in augmentation index was observed during the study (STG: 1.9% ± 16.0%, 1.4% ± 16.1%, and 2.0% ± 16.4%; CG: 0.2% ±

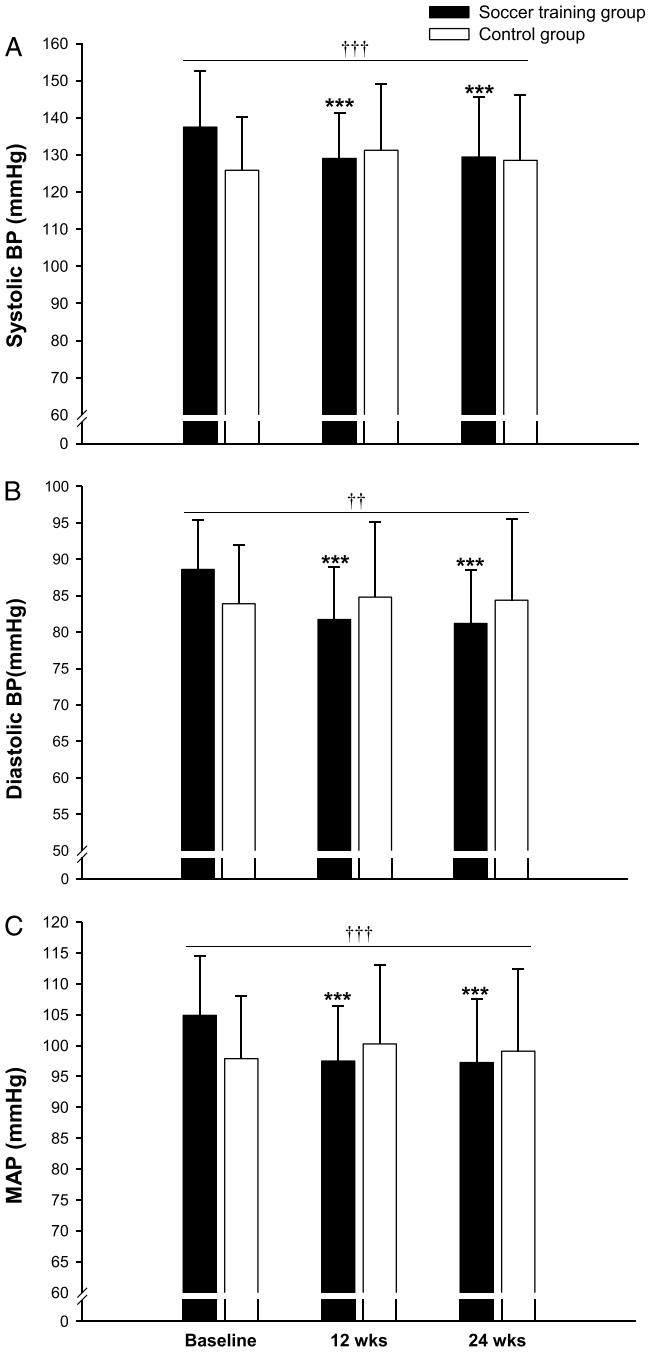

FIGURE 3—Systolic BP (BP) (A), diastolic BP (B), and mean arterial BP (MAP) (C) in men with T2DM before and after 12 and 24 wk of soccer training ($n = 12$) and controls ($n = 9$) with no change in lifestyle. ***$P < 0.001$, **$P < 0.01$ different from baseline; $^{\dagger\dagger\dagger}P < 0.001$, $^{\dagger\dagger}P < 0.01$ for significant interaction (time × group, ANOVA). Values are presented as mean ± SD.

13.6%, 0.2% ± 18.0%, and 0.8% ± 15.7% at baseline and after 12 and 24 wk, respectively).

DISCUSSION

The major findings of the present study were that 24 wk of regular soccer training improved cardiac structure and function, increased exercise capacity, and reduced BP in men with T2DM. The effects on LV diastolic function included improvements of *E*/*A* ratio, LV filling pressure, and peak early diastolic velocity. In particular, this is the first study to our knowledge to report improved myocardial systolic function after exercise training in T2DM patients. Indeed, we found a marked increase in LV longitudinal systolic function by TDI measurements and speckle tracking analysis together with improved right ventricular systolic function (TAPSE). Soccer training also markedly reduced BP and improved $\dot{V}O_{2max}$ and intermittent endurance capacity.

LV diastolic dysfunction was present at baseline in 75% and 33% of the participants in STG and CG, respectively, which is within the range of diastolic LV dysfunction prevalence observed in other studies of diabetes patients (6,13). We did not, however, detect pseudo-normalized transmitral inflow patterns in any subject, which is in contrast to other studies of asymptomatic T2DM patients without hypertension (6,13). This may suggest that the LV diastolic function alterations found in our study subjects were at an earlier stage, despite a mean T2DM duration of

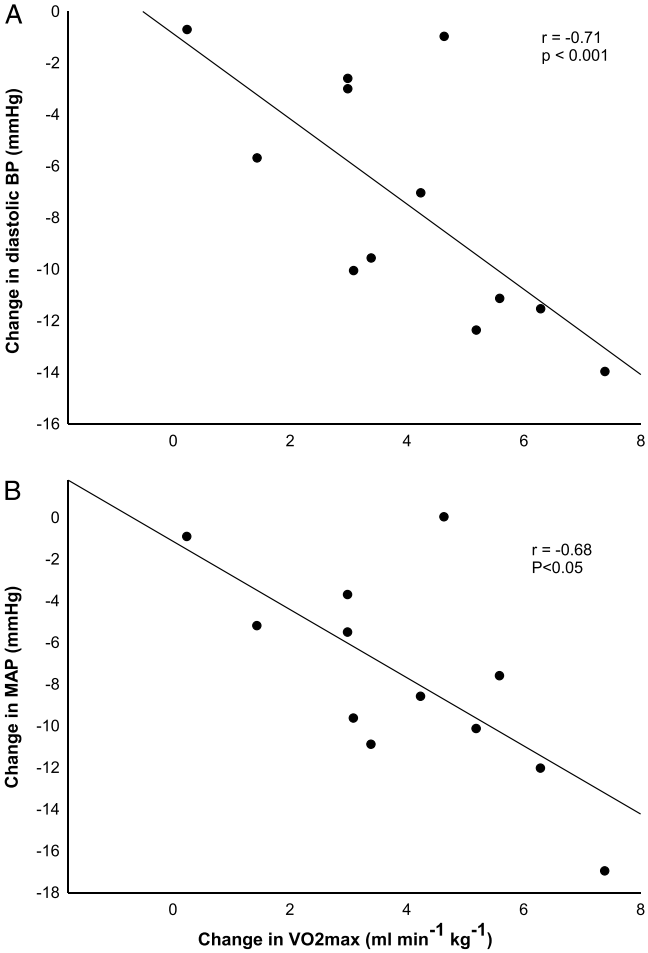

FIGURE 4—Individual relationship between changes in $\dot{V}O_{2max}$ ($mL \cdot min^{-1} \cdot kg^{-1}$) and diastolic BP (BP) ($r = -0.71$, $P < 0.001$) (A) and $\dot{V}O_{2max}$ and mean arterial BP (MAP) ($r = -0.68$, $P < 0.05$) (B) in men with type 2 diabetes after 24 wk of soccer training.

7 yr, potentially reflecting the aggressive multifactorial diabetes control practiced at the Steno Diabetes Center (16). Soccer training significantly increased E', E'_{TDIcolor}, and mitral inflow ratio (E/A ratio), indicating effective improvement of diastolic function. For example, E' improved in STG from 7 to 9 $\text{cm}\cdot\text{s}^{-1}$, which is similar to improvements found with intensive antihypertensive pharmacotherapy (37). Also, the effect observed in STG on peak diastolic velocity was comparable with changes observed after pharmacological glucose-lowering intervention, suggestive of a clinical relevance (39). Notably, the lower baseline values in STG compared with CG may have influenced the observed changes in diastolic function. However, the most important diastolic variables improved regardless of baseline values, while some variables changed more if lower baseline values were present.

Studies of effects of exercise training on diastolic function in T2DM are limited, and two studies found no change after 12 months of combined aerobic and strength training twice a week, although in one of these, subgroup analysis revealed that the time spent in vigorous exercise zones was related to favorable changes of diastolic function (21). On the other hand, other investigators found normalization of diastolic function after 12 wk of bicycling exercise three times per week. In all these studies, T2DM duration was considerably shorter than for our patients (9,21,27). Importantly, although improvements of LV diastolic function with exercise training may be more difficult to achieve in patients with long T2DM duration, we found marked improvements after 12 and 24 wk of soccer training in patients with relatively long (7 yr) T2DM duration, supporting that soccer training may be particularly effective in ameliorating LV diastolic dysfunction (4).

LV diastolic dysfunction has previously been considered to be the first marker of myocardial impairment in T2DM (32). However, with use of TDI, more recent studies have reported reduced longitudinal systolic LV function (S', strain, and displacement), even in the absence of diastolic dysfunction (5,13). Similarly, we found impaired longitudinal systolic function at baseline, but after only 12 wk of soccer training, we observed substantial increases of systolic TDI parameters together with markedly improved right ventricular systolic function (TAPSE). To our knowledge, the improvement of LV systolic function after exercise training in T2DM patients has not been reported previously, and these observations add to the notion that soccer training may exert beneficial effects on the heart (4). Reduced exercise capacity is common in T2DM patients and may contribute to reduced daily activity levels, compromised quality of life, and increased mortality. In STG, we observed significant improvements of exercise capacity in terms of increased $\dot{V}O_{2max}$ and intermittent endurance capacity, respectively, and these findings mirror results of a meta-analysis of beneficial effects of structured exercise interventions on cardiorespiratory fitness in T2DM patients (8). LV diastolic dysfunction can contribute to reduced exercise capacity, for example, by promoting a disproportionate increase in LV filling pressures during exercise, impaired myocardial perfusion, and reduced ability to increase stroke volume (7,22,33). Therefore, improved LV diastolic function in STG is likely to have significantly added to the increased exercise capacity observed in this group.

Coexistence of hypertension and T2DM is estimated to occur in approximately 80% of patients and nearly doubles the risk of cardiovascular events (17,38). Furthermore, BP reductions are generally accepted to be associated with markedly reduced risk of ischemic heart disease and death (26). In the current study, we observed reductions in systolic BP, diastolic BP, and MAP of 8, 8, and 8 mm Hg, respectively, after 24 wk of soccer training. These BP reductions are more pronounced than those reported after other exercise interventions in T2DM patients, where only 25%–30% of such BP reductions have been found (19). In addition, a 2007 meta-analysis found systolic/diastolic BP changes of 7/5 and 3/2.5 mm Hg in hypertensive patients and normotensive subjects, respectively, after dynamic aerobic exercise (14). The present findings, however, support previous results from our group, where marked BP reductions of 13, 8, and 10 mm Hg (systolic BP, diastolic BP, and MAP) were observed after soccer training in previously untrained hypertensive men, and somewhat smaller BP reductions were found in untrained men and premenopausal women, respectively (23–25). The target BP in T2DM patients is considered to be lower than 140/80 mm Hg (2), and tight BP control is of critical importance in patients with hypertension, for example, one study reported a 51% reduction of major adverse cardiovascular events with reduction of diastolic BP from <90 to <80 mm Hg (18). In STG, the BP was reduced from 137/89 to 129/81 mm Hg, and we observed strong associations between increases in $\dot{V}O_{2max}$ and reductions in diastolic BP and MAP (Fig. 4). Importantly, the reduction of BP observed in our patients is also likely to have contributed to the marked improvement of LV diastolic function (37). Also, increased arterial stiffness and endothelial dysfunction have been observed in persons with T2DM, which may contribute to elevated BP, LV diastolic dysfunction, and impaired prognosis (29). However, we found no changes in the augmentation index or the RHI in our study as measured by PAT, but more studies are clearly warranted to examine the mechanisms underlying the improvements of cardiac function and reductions of BP observed after soccer training.

In summary, 24 wk of regular soccer training improved myocardial systolic and diastolic function, increased exercise capacity, and reduced BP in middle-age men with T2DM. These favorable cardiovascular effects may be associated with reduced morbidity and mortality and warrant further studies of therapeutic and prognostic implications of soccer training in subjects with T2DM.

Limitations. Several limitations apply to the interpretation of our results. The study was nonrandomized, and the subject's possibility to select group assignment may have influenced the results. At baseline, all diastolic variables were lower in STG compared with CG, and randomization

may potentially have distributed these values more evenly. However, the improvements of diastolic function in STG remained significant after adjustment for the lower baseline values (ANCOVA analysis). Compliance with the intervention in STG (60%) was less than reported in previous soccer training studies (4,23–25), which may suggest that even larger improvements could have been achieved in a more compliant group of men with type 2 diabetes. Also, the study design is of importance, that is, increased training volumes after 12 wk may have provided additional benefits after 24 wk. The study subjects were middle-age men of Caucasian descent, and the results cannot be directly extrapolated to women, or to other age groups, and ethnicities. Moreover, apart from PAT measurements, mechanistic issues were not examined, for example, neurohumoral axis parameters and central hemodynamics.

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The authors declare no conflict of interest.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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