Cardiorespiratory function, atrial fibrillation and cardiovascular health effects of long-term endurance training in three different age groups of former or current long distance cross-country skiers.
A 28-30 year follow-up study.

'THE BIRKOPP STUDY'

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The famous "Birkebeiner Painting"

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List of papers

I. Grimsmo J, Arnesen H, Mæhlum S. Changes in cardiorespiratory function in different groups of former and still active male cross-country skiers: a 28 – 30-year follow-up study. Scand J Med Sci Sports 2010: 1(20): e317-e327
II. Grimsmo J, Grundvold I, Mæhlum S, Arnesen H. Echocardiographic evaluation of the aged male cross-country skiers. Scand J Med Sci Sports 2010: 10.1111/j.1600-0838.2009.01054.x
III. Grimsmo J, Grundvold I, Mæhlum S, Arnesen H. High prevalence of atrial fibrillation in long-term endurance cross-country skiers. Echocardiographic findings and possible predictors. A 28 – 30 year follow-up study. Eur J Cardiovasc Rehabil 2010: 17:100-105
IV. Grimsmo J, Mæhlum S, Mølstad P, Arnesen H. Mortality and cardiovascular morbidity among long-term endurance male cross-country skiers followed for 28-30 years. Submitted.

Abbreviations and definitions

AF: Atrial fibrillation
ANOVA: One-way analysis of variance
AV block degree I: Prolonged atrioventricular conduction time ≥ 220 msec
AVDO2max: Maximal arterio-venous O2 difference
BMI: Body mass index
CHD: Coronary heart disease
CI: Confidence interval
CO: Cardiac output
CTCS: Changed training time and/ or competing
CVD: Cardiovascular disease
DBP: Diastolic blood pressure
E/A: Early to late diastolic peak flow velocities
ECG: Electrocardiography
ESC: European Society of Cardiology
FEV1: Forced expiratory volume in one second
HbA1C: Glycated haemoglobin
HDL-cholesterol: High density lipoproteins cholesterol
HR: Resting heart rate
HRmax: Maximal heart rate
ICD: International classification of disease
IVRT: Intraventricular relaxation time
IVSd: End-diastolic anterior ventricular septal thickness
LAAs: Left atrial area in ventricular systole
LADs: Left atrial diameter in ventricular systole
LAF: Lone atrial fibrillation
LDL-cholesterol: Low density lipoproteins cholesterol
LVDd: End-diastolic left ventricular diameter
LVEF: Left ventricular ejection fraction
LVH: Left ventricular hypertrophy
LVPWd: End-diastolic posterior free wall thickness
MV: Minute volume = CO x HR
O2-pulse: VO2 in ml·min-1/HR in beats·min-1
PDA: Persistent ductus arteriosus
PQtime: Time in sec from the start of the p-wave to the start of the Q-wave.
RER: Respiratory exchange ratio
SBP: Systolic blood pressure
SBPmax: Maximal systolic blood pressure
SPSS: Statistical Package of Social Sciences
TC: Total cholesterol
TG: Triglycerides
UTSC: Unchanged training time and still competing
VC (FVC): Forced vital respiratory capacity
VO2max: Maximal oxygen uptake

Introduction

Background

The positive effects of regular physical exercise in the general population are well accepted (1). Regular physical exercise improves known cardiac risk factors as blood pressure, lipids and diabetes type II as well as reduces cardiovascular morbidity and mortality (2,3,4,5,6,7). Higher maximal oxygen uptake is an important factor that is related to decreased all-cause mortality (8,9).

Potential negative effects of chronic exercise training are still not fully understood or described in the litterature (10,11). It is known that short-term risk of sudden coronary events is increased during vigorous exercise, and coronary heart disease (CHD) is the main underlying cause of sudden cardiac death among the ageing adult athlete (12,13,14,15). However, in the studies by Lie et al., they did not find any increased risk of sudden cardiac death as a result of latent CHD among long-term endurance trained cross-country skiers followed after 5 and 7 years (16,17). In contrary, reduced mortality and longevity are described among former elite distance runners and cross-country skiers compared to the general population (18,19,20).

Bjørnstad et al. (21) and Pelliccia et al. (22) found no important potential dangerous changes to the heart among thirty former top-level Norwegian athletes aged 39 ± 3 years followed after 15 years or among young Olympic athletes with extreme and uninterrupted training over long periods up to 17 years, respectively. In contrary to this Baldesberger et al. found increased incidence of ventricular tachycardia, atrial fibrillation, sick sinus syndrome and atrial and ventricular dilatation in former professional cyclists (23). Hood et al. found that former marathon runners had left ventricular hypertrophy (24), while Jensen-Urstad et al. have reported high prevalence of ventricular arrhythmias (25).

Athlete's heart

Morphological changes (remodeling) of the heart as a result of long-term physical training are called the athlete's heart (26,27,28,29,30). For endurance athletes like cross-country skiers the adaptive changes to the heart include increased left and right ventricular and atrial cavity size and volume, and to a lesser degree left ventricular eccentric hypertrophy (31,32). Electrocardiographic changes in endurance athletes include sinus bradycardia, prolonged PR (PQ) interval (first and second degree AV-block), sinus arrhythmia, junctional escape rhthm, ventricular premature beats (PVCs) and elevation of the ST segment and J point (33,34). A more effective pumping heart is necessary to improve maximal cardiac output (COmax) in endurance athletes, because COmax is the single most important factor that limits VO2max in healthy people (35). Very high maximal cardiac minute volume (MVmax) is needed to supply the working muscles with enough blood during long-term endurance training and competing (36,37).

The ageing athlete

Maximal oxygen uptake (VO2max) is decreasing with increasing age both in endurance trained athletes and in the general population (38,39,40,41). Regular endurance training attenuates the decrease in VO2max in elderly people (42,43,44,45) and is important for

independent living at old age (46). However, MVmax is decreasing with increasing age also in those who still keep up rigorous regular training, as a result of both decreased maximal heart rate (HRmax) and COmax (40,46). The reduction in cardiac function and thus MVmax with ageing occurs mostly because of reduced cathecolamine sensitivity, prolongation of excitation-contraction time and intraventricular relaxation time (IVRT), increased afterload and increased vascular and myocardial stiffness with fibrosis (47,48,49). At the time of the initiation of the Birkopp study only three longitudinal studies describing changes in cardiorespiratory function with ageing with a follow-up time of more than 25 years were found in the literature (43,50,51). Only the study by Kasch et al. (43) demonstrated the cardiorespiratory changes in 5 endurance trained athletes, which made our longitudinal study with 68 athletes followed for almost 30 years quite exceptional.

Atrial fibrillation

The incidence of atrial fibrillation is increasing in western countries, mostly because of an older population and more survivors with cardiovascular disease (52,53). The prevalence of atrial fibrillation (AF) in the general population is less than 1 % among men younger than 40 years and increases up to more than 10 % in a population aged 75 years or more (54,55). The prevalence of so-called lone atrial fibrillation (56), which is AF without known structural heart disease or other known risk factors for AF, varies from 2 to 50 % of all with AF dependent on the chosen study population with AF (57,58,59).

At the initiation of the present thesis only 3 studies described a possible higher frequency of atrial fibrillation (AF) in athletes compared to the general population (60,61,62). Our interest in long-lasting sport practice and lone atrial fibrillation (LAF) started about 10 years ago, because of a rumour about rhythm disturbances among some middle aged and older Norwegian skiers competing in the Birkebeiner long-distance cross-country ski race. We had the unique possibility to investigate a group of former and still active cross-country skiers after almost 30 years (16,17,63).

Aims of the thesis

The general aim was to investigate the relation between long-term endurance training among cross-country skiers and positive and negative effects on cardiac structure and function after 28-30 years follow-up.

Specific aims

1. To assess longitudinal changes in cardiorespiratory function in different groups of current and former endurance trained male cross-country skiers. (Paper I).
2. To evaluate with echocardiography the effects of long-term endurance training on cardiac structure and function in three different age groups of 48 healthy middle-aged and old former or still active male cross country skiers. (Paper II).
3. To determine the prevalence of atrial fibrillation and lone atrial fibrillation in long-term cross-country skiers and to examine possible predictors. (Paper III).
4. To report the outcomes of mortality and cardiovascular morbidity and to investigate if known risk factors or ST-depression in an exercise test 25-years years earlier increased the risk of cardiovascular or coronary heart disease mortality or morbidity among a cohort of cross-country skiers followed for 30 years. (Paper IV).

Methods

Athlete population

The studies in 1976 and 1981
Approximately 34 years ago, 149 healthy males were invited to participate in a study. They were all long-time active, highly trained cross-country skiers belonging to three preselected age groups (group I: 26–33 years; group II: 43-50 years and group III: 58–64 years). Out of the 149 invited skiers 122 participated in the first study in 1976, with 35/48 from group I, 48/58 from group II and 39/43 from group III. The inclusion criteria for entering the study was that they 1) for several years had participated (among other races) in long-distance cross-country competitions (between 30 and 90 km), and 2) in general were among the ¼ with the highest performance in the various contests (62). Out of the 122 skiers, 117 (95.9%) participated in a 5-year follow-up study in 1981 (16). The examination program applied during the first and the 5-years follow-up study consisted of a physical examination, blood samples, vitalographic assessment, ECG registration during rest and exercise and a near maximal exercise test on an electrically braked Elema cycle ergometer (16,62). All subjects were interviewed about symptoms of cardiac disease and on exercise tolerance after 7 years follow-up. (17).

The 28-30 years follow-up study from 2004 – 2006
The men still alive from the original studies in 1976 and 1981 were asked to participate in a follow-up study. Out of the originally 122 subjects 37 had died during the period from 1976 to 2006, with 1/35 in group I, 8/48 in group II and 28/39 in group III. One in group I was not found in the central Norwegian national population register. Three from group II and three from group III did not respond to the invitation. Data were therefore available for 78 of the subjects still alive.

Paper I
Of the 78 still living men 68 (32 in age group I and 36 in age group II), who also participated in a cycle ergometer exercise test in 1976 were recruited for retesting and included in this study. The oldest 8 participants from age group III were excluded, because the Norwegian Ethical Committee did not approve maximal exercise testing in this age group. Two more subjects refused to do the exercise test at follow-up, because they had known coronary heart disease and were followed regularly at the local hospital and by a cardiologist, respectively.

Paper II
All together 75 out of the 78 still living subjects were recruited to an echocardiographic evaluation at Oslo University Hospital, Ullevaal. In the present study, we included 48 out of them (23 in age group I, 21 in age group II and 4 in age group III), while we excluded all with cardiac and/or pulmonary diseases and subjects on cardio active medication, which could interfere with the echocardiographic findings.

Paper III
Data on medical history including atrial fibrillation were available in all 78 participating subjects, with 33 in age group I (54 – 62 years), 37 in age group II (72 – 80 years) and 8 in

age group III (87 – 92 years). Diagnosis of atrial fibrillation was confirmed by ECG's or medical records, while the age of onset of AF was partly self-reported.

We used data both from 1976 and 1981 when looking for possible predictors of atrial fibrillation.

Criteria of LVH in 1976 and 1981 were according to the 'Scandinavian modification of The Minnesota Code for ECG classification' – MC 3.1-type: a)R amplitude 33 mm in either of leads CH 5, 6 or 7 and b) 20 mm in any of leads I, II, III or aVF, or c) 12 mm in lead aVL (63). ECGs were in 1976 and 1981 read blindly and PQ times were measured from the resting ECGs and noticed on the ECG's. Resting heart rates were measured after 10 minutes in the recumbent position (16,17). Echocardiographic data at follow-up were available in 75 of 78 subjects.

Paper IV

Cause specific death diagnosis and morbidity diagnosis in those still living were available in as many as 121 out of 122 subjects. Only one subject was missing and could not be traced in the Norwegian national population register. Cause-specific mortality data up to December 31st 2006 were obtained from death certificates provided by Norwegian National Registry. All death certificates were coded according to the *International Classification of Diseases* (ICD). Deaths between 1969-1985 and 1986-1995 were coded according to the Norwegian versions of ICD-8 and ICD-9, respectively, while deaths from 1996-2006 were coded according to the English version of ICD-10. Mortality and morbidity data from 1976 until follow-up in 2004-2006 or until the date of death were available in 115 subjects, and data from the Norwegian population register proved that the six men who did not respond to the invitation still were alive at the end of 2006. Longitudinal changes in TC, TG, HDL-cholesterol and TC/HDL ratio were assessed in subjects without medication with statins, with laboratory values both in 1976/1981 (n=59) and 2004-2006 (n=53).

Exercise testing and physical evaluation at follow-up in 2004-2006

Maximal exercise testing with ECG

After 10 minutes of moderate warming up all 68 subjects underwent a maximum exercise test on a "Woodway" treadmill (Marquette Electronics Case 15, Milwaukee, Wisconsin, USA), according to the modified Bruce protocol (65). This protocol had been used regularly in our cardiac rehabilitation unit at the Feiring Heart Clinic. In this protocol there was an increase in inclination and/ or speed every third minute. The first nine minutes were at constant speed 2.7 km/h with an increase in inclination to 5 % after three minutes and 10 % after six minutes. After nine minutes both speed and inclination were increased. Normal testing time varied widely among the participants (approximately from 13 to 20 minutes with the first nine minutes at a low working load). Metabolic and respiratory parameters were measured using a Sensor Medics Vmax 29 C-2130 Spirometer (Sensor medics Corp., Yourba Linda, California, USA).

The test was stopped when the subject reached VO2 maximum at exhaustion, or if ischemic or other ECG changes necessitated a premature break. The test was also stopped if the subject was not able to reach maximum for physical reasons, such as walking problems on the treadmill with increasing speed. Achievement of VO2max was accepted when a respiratory exchange ratio (RER) above 1.05 was present (66). All together 55 subjects reached VO2max. The highest heart rate at the end of the test was regarded as HRmax.

The electrocardiographic exercise test was performed following the guidelines of the European Society of Cardiology (67).

All tests were accomplished by the same experienced investigator (JG).

Vitalographic evaluation

A vitalographic assessment of forced respiratory vital capacity (VC) and one second forced expiratory volume (FEV1) was performed in 75 subjects.

Physical examination

The examination programme included a physical examination, (height, body mass, supine resting blood pressure, and heart and lung auscultation).

Blood tests

The blood tests in the two former studies included serum total cholesterol (TC), serum triglycerides (TG) and serum high density lipoproteins (HDL) (HDL only in the study in 1981). All samples were analyzed in the Central Laboratory of Oslo University Hospital, Ullevaal [16]. At follow-up in 2004-2006 the blood samples included TC, TG, HDL, and serum low density lipoproteins (LDL : calculated according to Friedewald's formula)) and long-time blood glucose (HbA1C) analyzed at Akershus University Hospital, Lorenskog for age group I and II and at Oslo University Hospital, Ulleval for age group III (the same methods in both laboratories).

Echocardiographic evaluation

Complete two-dimensional, M-mode and Doppler recordings at rest were obtained with a VingMed Vivid 7 (Vingmed Sound, Horten, Norway) echocardiograph. All recordings were obtained by one study investigator (IG) at the department of cardiology, Oslo University Hospital, Ulleval, using standard methods of measurements (59,68,69).

Questionnaire

The subjects answered questions about life-long training and competition patterns and history, identical to the questions answered in two earlier studies from 1976 and 1981 (16,17). In addition they answered questions about medical status including detailed questions about heart and lung diseases, smoking habits and health- and social status. The subjects also answered questions about dietary intake and quality of life (SF-36), which are not part of this thesis. Questions about training status were identical to those asked in 1976 and 1981.

Statistical analyses

Data analyses were performed with the Statistical Package for the Social Sciences, Chicago, IL, USA (SPSS 14, 2005 to SPSS 18, 2009), except from paper IV where the survival analyses were conducted with STATA software version 11 (College Station, Texas, USA). Data from 1976 were originally in paper version, and were carried over to the SPSS or STATA. A 'monitoring certificate' is given, which attests that data from a random sample of 20 % of all enrolled subjects in this study have been monitored and controlled. The exact use of statistical analysis is described in detail in each paper.

Differences between mean values were assessed with the unpaired Student t test if normally distributed; otherwise the Kruskal-Wallis test was used. Categorical variables were assessed by Fisher's exact test or chi-square test as appropriate. Data collected during initial and follow-up testing were used to determine longitudinal changes in the different cardiorespiratory variables and physical activity (paper I). One-way analysis of variance (ANOVA) was used to determine differences in the dependent variables among different pre-selected groups. Repeated-measures analysis of variance and/ or paired-samples t-test for repeated measures were used for assessment of changes over time within each group and differences between the age groups. The data were tested for normal distribution using quintile-quintile (QQ) plots. Correlations controlled for different variables (especially age) and multiple regression analyses were used to determine relations among variables. Univariate analyses of survival from all-cause mortality and survival free of CVD and/or CHD were performed using Kaplan-Meier product limit estimator and log-rank tests. Survival adjusting for baseline risk factors was evaluated in a multivariate Cox proportional hazard model. The Cox model was built by a forward selection procedure. The assumption of proportional hazards was checked using log-log survival plots and tests based on Schoenfeld residuals. Continuous covariates were evaluated for linearity in log hazard. Interaction terms were kept in the model if they were statistically significant and biologically interesting (paper IV). A p value < 0.05 was considered significant. Values are expressed as mean and standard deviation unless indicated otherwise.

Summary of results

Paper I

This paper described longitudinal cardiorespiratory changes with ageing in two different age groups and in subgroups among those who had unchanged training and competing status versus those who had changed either training or competing status or both. We found a significant difference in the decline in VO2max with ageing between age group I and age group II in % · decade -1 (8.8 ± 3.8 vs. 14.5 ± 3.7; p = 0.042) and in l · min -1 · decade -1 (0.48 ± 0.23 vs. 0.60 ± 0.18; p = 0.0001). Men in group I (but not in group II) who was still competing and reported unchanged training had an attenuated decline in VO2max in % · decade – 1 (6.5 ± 4.2 vs. 10.1 ± 2.8; p = 0.011) and in l · min -1 (0.35 ± 0.24 vs. 0.55 ± 0.20; p = 0.024). No single factor was found to be responsible for the change in VO2max. Thus, this study shows that lifelong endurance training does not stop the decline in VO2max with ageing, but vigorous training is important to attenuate the decline.

Paper II

This echocardiographic study evaluated the effects of long-term endurance training on cardiac structure and function in three different age groups of 48 healthy middle-aged and old former or still active male cross-country skiers (23 in age group I: age 58.6 ± 2.2 yrs; 21 in age group II: age 74.9 ± 2.2; 4 in age group III: age 89.5 ± 1.9). The two oldest age groups were combined and compared to age group I.

No significant differences in left atrial or ventricular dimensions between these two age groups were found. A high proportion of enlarged left atrial dimensions were found among all subjects with 80 % exceeding upper reference limit of 40 mm in diameter (LADs) and 94 % exceeding upper reference limit of 20 cm^2 in area (LAAs). Mean values for LADs (mm) and LAAs (cm^2) were; Group I: 41.9 ± 4.7 and 24.7 ± 3.3; group II: 43.5 ± 4.8 and 25.2 ± 3.7; group III: 44.5 ± 4.7 and 25.8 ± 3.7. Left ventricular diastolic diameter exceeded upper reference limits of >54 mm in 20 subjects among all. The groups had preserved systolic and age-related diastolic function.

We concluded that enlarged left atrial dimension seems very common among healthy endurance trained cross- country skiers and that there were no differences in atrial or ventricalar dimensions between the two compared age groups.

Paper III

In this study we sought to determine the prevalence of LAF in long-term endurance cross-country skiers and to examine possible predictors for lone atrial fibrillation.

We found a high prevalence (12.8 %) of LAF among the cross-country skiers, with 18.2 % in age group I. The only predictor from both 1976 and 1981 associated with LAF was a long PQ time (r = 0.38, p = 0.001 and r = 0.27, p = 0.02, respectively), while bradycardia was another predictor from 1981 (r = 0.29, p = 0.012). At follow-up left atrial enlargement assessed by echocardiography was a marker associated with LAF (p<0.001). We found about three times the risk of developing LAF among those with ECG criteria of LVH in 1981 (55 subjects) compared to those withoun (20 subjects). However, this difference was not statistically significant.

In conclusion, long PQ time and bradycardia from baseline (1976 and 1981) and left atrial enlargement at follow-up seem to be important risk factors for the increased risk of LAF among long-term endurance cross-country skiers.

Paper IV

In this paper we have described the outcomes of mortality and CVD morbidity after 30 years follow-up in long-term trained cross-country skiers and examined possible risk predictors for later appearance of CVD and CHD.

Total deaths were 31 % compared to 40 % in the general male population of Norway ($p = 0.04$). Exercise-ECG ST-depression in 1981 was associated with later appearance of CHD (HR 2.90; $p = 0.033$). BMI and average systolic blood pressure (SBP) from 1976/1981 were predictors of later appearance of CVD (HR 1.23; $p = 0.034$ and HR 1.03; $p = 0.048$, respectively). Among the still living (age 67.3 ± 8.3 yrs: range 51-92 yrs) low prevalence of CHD (14.1 %), diabetes type II (2.6 %), hypertension (11.5 %) and BMI > 30 (1.3 %), and favourable risk factors with 5.1 % smokers, high HDL: 1.8 ± 0.4 mmol/l, low total cholesterol/HDL ratio: 3.4 ± 1.0, and low SBP: 122 ± 13 mmHg, were found.

Long-term aerobic exercise appears to be associated with reduced all-cause mortality and morbidity and favourable CVD risk factors.

Discussion

It is well known that long term effects of exercise reduce all-cause mortality and cardiovascular (CVD) morbidity and mortality (9,17,70,71,72). Until recently mostly positive consequences of physical training for the heart have been demonstrated even though it is known that short-term risk of sudden coronary events is increased during vigorous exercise [13,14]. Only a few studies have found that former top-elite athletes have increased life expectancy, mostly because of reduced prevalence of CVD (18,19,20,73,74). Over the last years possible negative cardiac effects of long-lasting endurance competitions and long-term endurance training have been described among participants in triathlon, bicycling, marathon, 24-hours run and orienteering [10,11,75,76]. Most of the studies have evaluated the effects of extreme endurance training on ventricular function and rhythm (22).

The main findings of the present study are related to long-term effects of endurance training on the cardiorespiratory system and especially the heart. To date this is one of the longitudinal studies in sports cardiology and physiology with the longest follow-up time. We have shown that (i) maximal oxygen uptake decreased with increasing age, but the decrease was significantly lower in those reporting unchanged training habits and were still competing versus those who had reduced training time per week and/or had stopped competing (paper I), (ii) cardiac adaptive changes in healthy still active or former cross-country skiers included borderline enlarged ventricular dimensions and eccentric hypertrophy (athlete's heart) and enlarged atrial dimensions, and these changes were not different between an older versus a younger age group (paper II), (iii) lone atrial fibrillation was much more common among this endurance trained population than reported among men in the general population, and bradycardia, long PQ-time and enlarged atrial size were predictors for later appearance of LAF (paper III) and (iv) long-term endurance cross-country skiers in our population live longer than males in the general population, they had favorable risk factors for CVD, but still CVD was the most common cause of death among all and among those dead younger than 80 years old (paper IV).

Methods

This longitudinal cohort-study did not have any sedentary control group or a control group from the general male population, which could have made this study even more unique. Thus, we had to base our comparisons on data described in the literature or on data found in the Norwegian national population register. We also had to use the subjects as their own controls, by sub-grouping the population.

One problem by sub-grouping a population of relatively few subjects is that there may be too few subjects to do meaningful statistical analysis, or that it could lead to statistical type II error, selection bias or confounding. These statistic problems are described as study limitations in the different papers in the thesis.

Long-time longitudinal cohort studies and exercise testing

One major limitation to our study (paper I) was the different methods of estimating VO2max, HRmax and other ergospirometric measures in the baseline studies from 1976 and 1981 and in the follow- up study in 2004-2006. The problem of using an indirect measure of VO2 max from a cycle ergometer test at baseline compared to a direct measure method from a treadmill test at follow-up has been thoroughly described under methods in paper I. It was not found

proper to use the same indirect test at follow-up as at baseline, because of the uncertainty by using this test in older age groups and the described relatively large method error (37,77).

The direct method of measuring peak oxygen uptake (called VO2max in the different papers) is to day the golden standard of demonstrating exercise capacity (78). We used the modified Bruce protocol as described under methods, which is a standard testing procedure in coronary heart patients (65). The use of this protocol in an older population consisting of both healthy subjects and subjects with different diseases can be criticized, because of the non-linear increase in load and high incline at higher loads (14 % incline and 6.7 km/h after 12 minutes), leading to leg exhaustion before reaching cardiopulmonary limitation. However, we choose to use the same protocol for all, even if testing time was somewhat shorter or longer for some subjects (varied between 4 and 11 minutes after the first 9 minutes warming up) than recommended for maximal exercise testing (≈ 7 minutes) (79). In addition, we were familiar with the Bruce protocol and choose this because we tested an older population that could have different unknown cardiopulmonary diseases. We also choose the Bruce protocol as the better choice because there was no specific recommended testing procedure or protocols for older age groups of former athletes like in our study.

Longitudinal studies and other measurements

We were not able to assess the decrement in HRmax with ageing, because the subjects most probably did not reach their maximal heart rate during ergometer cycle testing at baseline, as described under methods in paper I. Thus, we could not include this important parameter in the multivariate regression analysis describing possible responsible factors for the decline in cardiorespiratory function with ageing.

As described in paper IV different laboratory methods in measuring blood lipids from baseline to follow-up could lead to some variability. However, the laboratory method at baseline was the standard method at that time and also used in the Oslo Study (107), and the method at follow-up was the same in all subjects (at Oslo University Hospital and Akershus University Hospital, respectively), indicating that the variability should be acceptable. In fact there is no other way to describe changes over time in long-term longitudinal studies.

Echocardiographic assessment at follow-up

The echocardiographic assessments were performed by one experienced specialist in cardiology using standard methods of measurements. Thus, we think that the measurements were correct and by the best standards. However, to be even more precise the golden standard would have been to have a second investigator to do another measurement from the echocardiographic files, both to look into inter-investigator variability and to double-check the measurements.

In addition, at the time we did the echocardiographic study it was not usual to calculate atrial volumes, but only atrial dimensions in diameter and area. Left atrial volume index is the preferable measurement of atrial size today (80). Unfortunately, we did not have baseline echocardiographic data that probably could have told us something about longitudinal changes in cardiac structure with ageing and/or detraining in subgroups.

Former files from the limited echocardiographic evaluation of 42 subjects in 1981 were lost in a hospital (Rikshospitalet) moving (81).

Results

The Birkebeiner population

All of the men were recruited from the Birkebeiner cross-country race. The skiers had several years with long-distance endurance training before the first study in 1976, and they had in general been among the 25 % best in the different contests (63). Most of them had continued to train and compete for many years after the second study in 1981 (16).We have in paper I and II shown that most of the men had a lifestyle with life-long physical exercising. Of the still living 78 subjects in the follow-up study in 2004 – 2006 only 2 of 32 had stopped training in age group I, while 6 of 36 had stopped training in age group II. Even if all 8 subjects in age group III reported that they had stopped training, they were still active with walking and to a lesser degree cross-country skiing at an age of approximately 90 years (data not shown in the papers). Half of the subjects in age group I were still competing compared to 6 subjects in age group II. In average each of these subjects had approximately accumulated 15.000 training hours. They had been training for about 39, 46 and 54 years in the three different age groups, respectively (papers II and III). Thus, they were very suitable for studying what happens to the master athlete with ageing (82).

Long-term long-endurance training and cardiovascular adaptation/ cardiac remodeling

Long-term endurance training leads to improved performance due to enhancements in cardiac function, muscle oxidative capacity and improved technical skills (35,37,83). We have shown that the Birkebeiner population in age group I and II had a very high VO2max with approximately 170 % of expected normal age-related values (paper I). Those men still competing at follow-up had an oxygen uptake as high as 185 % of expected (data not shown). Long-term high intensity training is necessary to achieve a high VO2max, which in turn is dependent on a high CO and MV (38). To support the muscular oxidative metabolism during long-term high intensity exercise large left ventricular filling and ejection is necessary (37). We (paper II) and others (32,84) have demonstrated that endurance training leads to cardiac morphological changes called the athlete's heart. In our old population of still active and former cross-country skiers as in other endurance trained athletes these changes included increased left and right ventricular and atrial dimensions and to a lesser degree left ventricular eccentric hypertrophy.

No difference in atrial or ventricular dimensions were found between two different age groups of approximately 58 and 78 yrs, indicating no reverse cardiac remodeling in older age with reduced training and competing time (paper II). In our relatively small age groups it was not statistically appropriate to assess the effects of detraining on cardiac structure and function (paper II). However, others have found incomplete cardiac reverse remodeling in former athletes after long-term deconditioning (85,86), supporting our findings.

We have shown that maximal oxygen uptake was decreasing with increasing age (paper I), as also shown in many studies both among athletes and in the general population (87,88,89). There seems to be an accelerated or higher decline in VO2max with increasing age as also shown by others (46). We did not find any single factor responsible for the higher decline at older age, but reduced pulmonary function, more persons with different health problems, reduced exercise induced cardiac chronotropy and inotropy (lower HRmax and CO), reduced training time and intensity and reduced muscle mass may contribute (44,50). However, we did not have data on maximal stroke volume, training intensity or lean body mass. We only had data on longitudinal changes in HRmax, pulmonary function (VC and FEV1), BMI and training time in hours per week. The decline in maximal O2-pulse (reduction in maximal

stroke volume and/or arterio-venous O2 difference), VC, FEV1 and HRmax were significantly greater in age group II compared to age group I (paper I). Cardiac function is decreasing with increasing age, as also shown among our population of cross-country skiers. Both stroke volume and diastolic function (E deceleration time, E/A ratio and IVRT) at rest are strongly decreasing with increasing age as shown in paper II, which in many studies is shown to be due to reduced cardiac and arterial muscular elasticity (increased afterload) and conduction time (excitation-contraction time) (49,50).

For a long time it has been questioned if the decline in VO2max with ageing is the same in endurance trained as in sedentary men (40). We found a lower decline per decade in age group I, but not for age group II, with 7 % in age group I vs. 10 % reported among men in the general population in the literature and 14 % in age group II vs. 15 %, respectively.

We have also shown that rigorous exercise training (in those who are still competing) is the strongest factor to reduce the age-related decrease in physical fitness with ageing. The decrease, as presented in paper I, was as low as 4 % per decade among those still competing and with reported unchanged training patterns through 28-30 years in age group I, which is about the same as has been shown among other still active master athletes (80,81), but lower than reported among males in the general population (90,91). Only 4 subjects in age group II reported unchanged traning and competing status through 30 years. We did not find the same age-related reduction in the decline in VO2max among them, which however could be due to statistical type II error.

Unfortunately we did not have former eccocardiographic measurements, which could have said something about cardiac reverse remodeling and detraining in the different age groups.

LAF

We (paper III) and others (92,93) have recently demonstrated that long time endurance training results in lone atrial fibrillation in many middle aged and old male athletes like cross-country skiers, marathon runners, former professional bicyclists and orienteers. Others have not found this negative consequence of training for the heart among younger athletes (21,94). It is suggested that exercise induced atrial fibrillation may be an even greater problem in the future, because more and more middle aged and older men (and to a lesser degree women) are participating in long-lasting endurance competitions and are practicing endurance training for many hours per week for decades. From the official result lists from the most popular long-distance cross-country race in Norway (the 54 km long Birkebeiner race) we found that as many as almost 8000 men and women (6629 men and 1364 women) at the age of 40 yrs or more participated in the race in 2010. In 1970 only 450 men over the age of 40 yrs took part in the competition, while women were not allowed to participate at that time. Our results were later confirmed in another study: “The Birkebeiner Aging Study: Self-reported Atrial Fibrillation (AF) in Old Athletes”, where 14 % of the 414 participants, aged 65 years and older, in the Birkebeiner ski race in 2009 reported paroxysmal or chronic atrial fibrillation (95).

LAF and atrial remodeling

In paper II we have found that > 80 % of healthy middle-aged and old current or former cross-country skiers without cardiovascular or pulmonary diseases had enlarged atrial dimensions. Atrial remodeling with enlarged dimensions seems to be a consequence of endurance training and competing, because of the high volume overload (increased preload) and cardiac output needed for long periods over time. In addition to enlarged atrial dimensions, slow heart rate because of pronounced parasympathetic tone and long atrioventricular conduction time seems

to be risk factors for developing atrial fibrillation after many years with endurance training as shown in paper III.

Another aspect to consider is that atrial dimension seems to increase with increasing age among the general population, as shown in a recently published study by Nan-Hung et al. (96). Echocardiographic measurements of normal atrial sizes in the general healthy older Norwegian population are scarce. However, we found the same enlarged atrial dimensions also among the youngest age group, indicating that the changes were a result of endurance training and not only ageing. This is also supported in the study by Hoogsten et al. (97), where they found that atrial remodeling with dilatation started already in 17-year old athletes and was further increased in 29-year old athletes. In another recently published study Baggish et al. (98) found larger atrial volumes among elite rowers compared to subelite rowers. Both groups had larger volumes than controls.

Morbidity and longevity

In our material of 121 former and still active long-endurance cross-country skiers in three different age groups we have found (paper IV) that they live longer than males in the general population and have lower prevalence of diabetes, hypertension, CVD and most probably also of cancer. This supports the former findings in many studies about the positive effects of exercising on known risk factors for CVD including diabetes (2,99), and on the risk for cancer (100,101). However, by including only long-term cross-country skiers in the first study in 1976 we can not exclude a selection bias. Our results may therefore not be representative among men in the ordinary population (73).

One important positive 'side' effect of participating in training and competitions is that almost none of the subjects smoked. Smoking is a strong risk factor both for CVD and cancer (102,103,104). The number of smokers was found to be very low (5 %) compared to the general male population (> 20 %). Even if total cholesterol (TC) was about the same as in the general population at the same ages, we found that the TC/HDL (high density lipoprotein)-ratio was relatively low in our population with 3.2 compared to values in the general population (Paper IV). Physical exercise is one of few factors that raise the HDL level (105,106).

No one in our material died suddenly during competitions, even if it is well known that sudden cardiac deaths appear in long-distance cross-country races like Vasaloppet (15). Only one person (paper IV) may have died during training, while the only one dead in the youngest age group died several hours after a training session. All together these subjects had far more than 1 million lifelong training hours, demonstrating that the risk for sudden death during training among the cross-country skiers in this population was extremely low as described in younger athletes (107,108,109). The protective effects of exercise training on known risk factors for CVD exceed the small risk of suffering sudden cardiac death, as also shown in other studies (14). However, in paper IV it is shown that CVD was the main cause of death among the cross-country skiers as among men in the general population. This result could partly be the cause of a reduced cancer frequency as a result of long-term exercising (95,96). Life-long participation in endurance training and competitions does not fully protect against the atherosclerotic process leading to CVD at older ages, which is a complex process including multi-factorial components (110,111).

Perspectives

All recommendations in cardiac primary and secondary prevention programs encourage people to live an active life with daily physical activity (3). There is so far no need to change the normal activity level recommendations among the general population as a result of the present or other studies. In contrary, all physicians should encourage inactive and moderate active men and women at any age to increased activity level, because physical inactivity is a major problem of increasing importance in most countries today. Encouraging men and women to participate in moderate to hard physical activity most of the days/week is good medicine; it is safe and gives health benefits.

However, we have to ask whether it is time to give warnings against long-term intensive endurance exercise after for example the age of 50 yrs, because of the increased risk of atrial fibrillation. Still, we do not know the dose-response curve for the increased risk of atrial fibrillation among long-term endurance athletes. Many unanswered questions still remain. We do not know for how many hours and for how many years one has to train to have an increased risk. Neither do we know if women have the same risk as men, or if they are more protected because of smaller cardiac dimensions or other not known reasons. We do not know if we have to practice endurance training at high intensities to have the increased risk for atrial fibrillation or other negative effects of cardiac remodeling. At last we do not know if there are individual genetic factors predisposing to atrial fibrillation in athletes.

The available evidence of negative effects of long-term endurance sports for the heart is still contradictory. Most of the studies available are small case-control studies or longitudinal cohort studies including a limited number of mostly male participants. The lack of studies in sports cardiology in women is disappointing. We need more longitudinal studies in large populations of male and female long-term endurance athletes compared to control groups of an inactive population and a less active population to answer the still remaining questions. Until then we have to take care of the athletes who have developed a negative cardiac consequence as LAF of long-term physical activity by giving them the best available treatment today, either by detraining and regular follow-up, medical treatment or possibly pulmonary vein ablation (112,113).

Finally, if the CHAD 2 score for the risk of embolic events in AF also holds true for this population should be investigated (114).

Conclusions

- Cross-country skiers from the Birkebeiner population have almost without exception a lifestyle with life-long endurance training resulting in high physical fitness at older ages (Paper I).

- Life-long endurance training does not stop the decline in VO2max with ageing, but vigorous training probably contributes to attenuate the decline (Paper I).

- No single factor was found to explain the decline in VO2max with ageing, but reduced training intensity, reduced HRmax and cardiac output, more health problems, reduced pulmonary capacity and BMI may contribute (Papers I and II).

- Long-term cross-country 'Birkebeiner' cross-country skiers developed 'athlete's heart', which consist of enlarged left atrial and ventricular dimensions and eccentric ventricular hypertrophy, but still normal systolic and diastolic cardiac function. A very high frequency of atrial enlargement among all, and no difference in cardiac dimensions between the different age groups were found (Paper II).

- A high prevalence of lone atrial fibrillation (LAF) among all still living cross-country skiers was found. Long PQ-time, low resting heart rate and left atrial enlargement seem to be important risk factors for the increased risk of LAF among long-term endurance trained cross-country skiers (Paper III).

- Long-term endurance male cross-country skiers were found to live longer than males in the general population; they also had low prevalence of diabetes, obesity, hypertension, cardiovascular disease (CVD) and cancer. In addition they had favourable risk factors for CVD with few smokers, low systolic blood pressure and favourable TC/HDL-cholesterol ratio (Paper IV).

- Age was the only predictor of all-cause mortality. ST-depression in an exercise test 25 years earlier was a predictor of fatal or non-fatal coronary heart disease, while higher systolic blood pressure and higher BMI was predictors for later CVD mortality and morbidity (Paper IV).

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Changes in cardiorespiratory function in different groups of former and still active male cross-country skiers: a 28–30-year follow-up study

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The aim of the study was to assess longitudinal changes in cardiorespiratory function in different groups of current or former endurance trained male cross-country skiers. Three different age groups ($n = 122$) took part in a similar study in 1976. Of 86 men still alive 78 responded (90.7%). Thirty-two from group I (age 58.7 ± 2.3) and 36 from group II (age 74.5 ± 2.5) participated in a maximum exercise test. We found significant difference in decline in VO_{2max} between age groups (%/decade: 6.7 ± 3.6 vs 13.9 ± 3.2; $P = 0.0001$ and in L/min/decade: 0.32 ± 0.18 vs 0.53 ± 0.14; $P = 0.0001$). Men in group I (but only a tendency in group II) who were still competing and reported unchanged training patterns had a significant attenuated decline in VO_{2max} (%/decade: 4.1 ± 3.7 vs 8.1 ± 2.8; $P = 0.003$ and L/min: 0.19 ± 0.0.17 vs 0.39 ± 0.15; $P = 0.004$). This study shows that lifelong endurance training does not stop the decline in VO_{2max} with ageing, but vigorous training is important to attenuate the decline.

Little is known about the specific mechanisms responsible for the decline in cardiovascular fitness with aging in humans. The age-related decline in VO_{2max}, however, is well documented (Åstrand, 1960; Åstrand et al., 1973). Most of the studies for men are cross-sectional (Saltin & Grimby, 1968; Dehn & Bruce, 1972; Shvartz & Reibold, 1990; Talbot et al., 2000; Pimentel et al., 2003). Longitudinal data are rare, but some studies have described the decline in VO_{2max} with increasing age in endurance-trained older men (Rogers et al., 1990; Hagerman et al, 1996; Trappe et al., 1996; Kasch et al., 1999; Katzel et al., 2001; Wiswell et al., 2001) and in the general healthy older male population (Åstrand et al., 1973; Rogers et al., 1990; Pollock et al., 1997; Stathokostas et al., 2004). Physiological changes with ageing (decreases in maximum heart rate, stroke volume and arteriovenous O_2 content difference during maximum exercise), reduction in training time and/or training intensity, gain of body mass, reduction in muscle mass and reduced health status have been supposed to be responsible for the decline in VO_{2max} (Stratton et al., 1994; Toth et al., 1994; Åstrand et al., 1997; Johnson et al., 2000). Changes in lung elasticity (chest wall compliance and elastic recoil of the lung) and impaired gas exchange with ageing are supposed to be responsible for the decrease in forced vital respiratory capacity (VC) in athletes as well as in non-athletes from middle age (Levin et al., 2007). Oxygen uptake is related to VC, in the way that those with the highest VC also normally have the highest maximum oxygen uptake. However, the individual range of distribution is wide, because VC is closely correlated to body size (Janssens et al., 1999; Åstrand et al., 2003, Ref. 1).

Only three longitudinal studies with a follow-up time for more than 25 years were found in the literature (Åstrand et al., 1997; Kasch et al., 1999; McGuire et al., 2001a, b), with 26 (former physical education students), 11 (endurance trained) and 5 (non-athletic) males, respectively.

In the present study, a follow-up has been carried out after 28–30 years on 68 still living subjects previously studied in 1976 (Lie & Erikssen, 1978). The aim of the study was to assess longitudinal changes in cardiovascular and respiratory function with ageing in two different age groups according to training and competing status, and examine possible responsible factors for the change over time.

Materials and methods

Approximately 30 years ago, 149 healthy males were invited to participate in a study. They were all long-time active, highly

trained cross-country skiers belonging to three pre-selected age groups (group I: 26–33 years, group II: 43–50 years and group III: 58–64 years). Out of the 149 invited skiers 122 (81.8%) participated in the first study in 1976, with 35/48 (72.9%) from group I, 48/58 (82.6%) from group II and 39/43 (90.7%) from group III. The inclusion criteria for entering the study was that they (1) for several years had participated (among other races) in long-distance cross-country competitions (between 30 and 90 km) and (2) in general were among the 1/4 with the highest performance in the various contests (Lie & Erikssen, 1978). Out of the 122 skiers, 117 (95.9%) participated in a 5-year follow-up study in 1981 (Lie & Erikssen, 1984). The examination program applied during the first and the fifth to seventh years follow-up study consisted of a physical examination (not specified), vitalographic assessment, ECG registration during rest and exercise and a near maximum exercise test on an electrically braked (Elema Schönander) cycle ergometer (Lie & Erikssen, 1978, 1984).

The men still alive from the original study were asked to participate in this present follow-up study. The Norwegian Regional Ethical Committee approved the study protocol, after exclusion of the oldest age group III from exercise testing. Permission was given from the Norwegian Data Inspectorate and the Norwegian Board of Health. All of the participants provided informed consent to the approved study protocol.

Out of the originally 122 subjects 37 (30.3%) had died during the period from 1976 to 2006, with 1/35 in group I, 8/48 in group II and 28/39 in group III. One in group I was not found in the central Norwegian national register. Three from group II and three from group III did not respond to the invitation. Data were therefore available for 78 (92%) of the subjects still alive. Two men from groups I and II, respectively, did not want to do the physical tests, but answered the questionnaires and gave permission to look into their medical reports. Seven out of eight from group III answered two questionnaires, and data from medical reports were available for the last one, who did not answer the questionnaires. Five subjects from group III participated in vitalographic assessments.

Sixty-eight men (32 in group I, 36 in group II), who also participated in a cycle ergometer exercise test in 1976 were recruited for retesting and included in this present study. A flow-chart for participating and missing/excluded subjects is shown in Fig.1.

Questionnaires

The subjects answered questions about training and competition status, dietary intake, smoking habits and health and social status. Questions about training status were identical to those asked in 1976 and 1981.

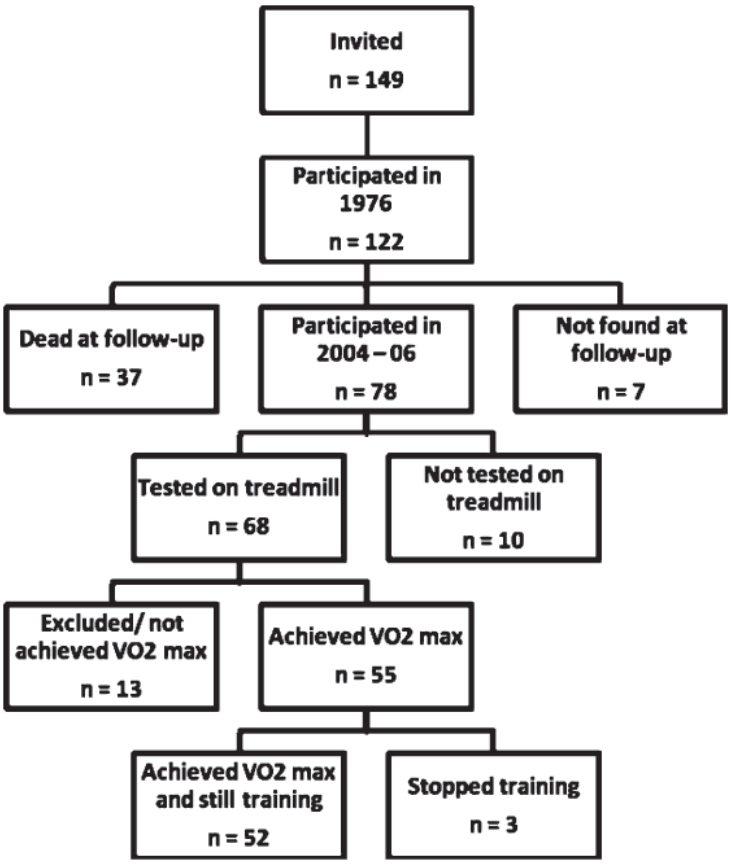

Fig. 1. Flow-chart for participating and missing/excluded cross-country skiers from baseline to follow-up.

Physical examination and exercise testing

The examination program included a physical examination, (height, body mass, supine resting blood pressure, heart and lung auscultation), a vitalographic assessment of forced respiratory VC, one second forced expiratory volume (FEV_1) and a maximum treadmill exercise test with ECG.

After 10 min of moderate warming up, all 68 subjects underwent a maximum exercise test on a 'Woodway' treadmill (Marquette Electronics Case 15, Milwaukee, Wisconsin, USA), according to the modified Bruce protocol (Bruce, 1978). This protocol is used regularly in our cardiac rehabilitation unit. In this protocol, there will be an increase in inclination and/or speed every third minute. The first 9 min are at constant speed 2.7 km/h with an increase in inclination to 5% after 3 min and 10% after 6 min. After 9 min both speed and inclination are increased. Normal testing time will vary widely (approximately from 13 to 20 min with the first 9 min at a low working load). Metabolic and respiratory parameters were measured using a Sensor Medics Vmax 29 C-2130 Spirometer (Sensor medics Corp., Yourba Linda, California, USA).

The test was stopped when the subject reached VO_{2max} at exhaustion, or if ischemic or other ECG changes necessitated a premature break. The test was also stopped if the subject was not able to reach maximum for physical reasons, such as walking problems on the treadmill with increasing speed. Achievement of VO_{2max} was accepted when a respiratory exchange ratio (RER) above 1.05 was present (Helgerud et al., 2007). The highest heart rate at the end of the test was regarded as maximum heart rate (HR_{max}).

The electrocardiographic exercise test was performed following the guidelines of the European Society of Cardiology (ESC Working Group, 1993).

All tests were accomplished by the same experienced investigator (J.G.).

VO_{2max}, HR_{max} and $O_{2\ pulse}$ in 1976

The subjects in age groups I and II participated in a near maximum cycle ergometer test in 1976 (Lie & Erikssen 1978). The starting load was 200 W (1200 kpm/min) for 6 min, directly followed by 6 min on 250 W (1500 kpm/min). Thereafter the men had 2 min rest and started at 300 W. Then the load was successively increased by 50 W (300 kpm/min) every third minute. The exercise test was continued until exhaustion. VO_{2max} was in 1976 predicted according to Åstrand and Rhyming (1954) with correction factor for age (Åstrand I. 1960) using data from load 2 (250 W).

A major problem in this study was the difference in VO_{2max} assessments between baseline in 1976 and follow-up in 2004–2006. VO_{2max} from 1976 was presented according to Åstrand and Rhyming in the original paper by Lie & Erikssen (1978). However, prediction according to this method is associated with a relatively large method error, with a standard error of about 10% in relatively well-trained individuals (Åstrand et al., 2003, Ref. 2). Very well-trained persons are often overestimated and older age-groups of men (41–46 years) could be underestimated by as much as 12% (Åstrand et al, 1973).

In this study, the subjects performed a near maximum cycle ergometer test in 1976, and we therefore had the maximum performance in watts, which usually is better correlated to the measured maximum oxygen uptake than is the values derived from data obtained during submaximum testing (Edgren et al., 1976). Therefore, we calculated VO_{2max} from maximum power output (watt) in the two different age groups by using the equations by Andersen et al. (1987) for male subjects (range 16–19 years) and Andersen (1995) for both genders (mean age 20, range 15–28 years). The maximum load on which the participants were able to perform exercise for one full minute was selected as maximal load in watts. We did not find any difference between the two equations, but the assessments by using these equations in our age groups obviously gave too low values with an average VO_{2max} of 4.3 ± 0.4 L/min (vs 5.2 ± 0.7 L/min according to Åstrand & Rhyming) in age group I and 3.8 ± 0.3 L/min (vs 4.0 ± 0.5 L/min according to Åstrand & Rhyming) in age group II. For age group I expected values for skiers of international calibers would normally be more than 80 mL/kg/min among highly trained male cross-country skiers (Hoff et al., 2002), who are among the athletes with the highest VO_{2max} (Åstrand et al., 2003, Ref. 3). However, as a group the skiers in this present study were not of international caliber, judging from the data on training hours per week. Therefore, we should expect markedly lower values than for top athlete skiers. For age group II the results of VO_{2max} are probably somewhat underestimated by both methods. A difference in age of 16.5 years between age groups in 1976 gives a difference in VO_{2max} of 1.2 L/min according to Åstrand and Rhyming (with age correction), while a difference of 12.3 years between age group II in 1976 and age group I at follow-up (the latter by direct measurement of VO_{2max} including subjects who had stopped training and reduced training hours per week) only gives a difference of 0.3 L/min (see Table 2 for data in 2004–2006). Using VO_{2max} estimated from maximum power output only gives a difference of 0.1 L/min.

Another test using maximum power output is the W_{max} 6-min test (Nordesjø, 1974). We did not find this test useful in our two different age groups of cross-county skiers of three reasons: (1) because of older age groups in our study, (2) because of different ways of performing the maximum tests and (3) because the test has not been proven to be significantly more accurate in estimating VO_{2max} than the sub maximum test by Åstrand and Rhyming (Edgren et al., 1976).

Another important aspect is that VO_{2max} values attained on a cycle ergometer usually are 5–11% lower than those measured during treadmill running (Hermansen & Saltin, 1969; Strømme et al., 1977). The values derived on the cycle ergometer in 1976 could therefore be lower than treadmill values. However, when adding $\approx 8\%$ to the VO_{2max} values from 1976 the new results do not affect the data to an extent that might alter the conclusions in this study.

HR_{max} is biased (too low) in 1976 even if HR_{max} was obtained at the end of the test at exhaustion or leg fatigue (see Discussion). The relatively low mean values for peak heart rate indicates that maximum oxygen uptake was not attained.

Among the two methods applicable in the study from 1976 it is very likely that one is overestimating, while the other is underestimating maximum oxygen uptake (especially among men in the youngest age group I). There is not enough evidence for choosing one before the other. Consequently, we have chosen to use the average of the two methods as the better choice in this present study, even if VO_{2max} in age group II most probably is somewhat underestimated in both. The absolute numbers of VO_{2max} in 1976 and longitudinal decline in VO_{2max}, but also the comparison between age groups I and II, must be interpreted with caution in this study.

$O_{2\ pulse}$ is assessed from VO_{2max} and HR_{max} at the end of the test. The biased maximum heart rate in 1976 invalidates assessment of heart rate changes from 1976 to 2004–2006 and their effect on change in VO_{2max}. $O_{2\ pulse}$ from 1976 may also be biased because of biased HR_{max} and the method of assessing VO_{2max}.

Exclusion criteria

Nine subjects (two from group I and seven from group II) who did not achieve VO_{2max} ($RER < 1.05$) were excluded from the assessment of decline in VO_{2max}. Four more subjects (all in

group II), who achieved RER > 1.05 were excluded; one because of atrial fibrillation during the treadmill test, one because he had an implanted pacemaker and two others because they used β-blockers. Six men treated for hypertension and five men with treated and stable coronary heart disease were included, because they felt healthy and did not use medication, which is supposed to interfere with the results to any appreciable extent.

Statistical analysis

Data analysis was performed with the Statistical Package for the Social Sciences version 14 (SPSS 14, 2005). Data from 1976 were originally in paper version, and were carried over to the SPSS. A 'monitoring certificate' is given, which attests that data from a random sample of 20% of all enrolled subjects in this study have been monitored. Data collected during initial and follow-up testing were then used to determine longitudinal changes in the different cardiorespiratory variables and physical activity. One-way analysis of variance (ANOVA) was used to determine differences in the dependent variables among different pre-selected groups. Repeated-measures analysis of variance and/or paired-samples *t*-test for repeated measures were used for assessment of changes over time within each group and differences between the two age groups. The data were tested for normal distribution using quintile–quintile plots. Correlations controlled for age and multiple regression analysis were used to determine relations among variables. A *P*-value <0.05 was considered significant. Values are expressed as mean and SD unless indicated otherwise.

Results

Results among all 68 subjects from age groups I and II

Age group I had gained some more weight than age group II, but not significantly ($P = 0.09$). Both groups had reduced their training hours per week from baseline to follow-up, but the change in hours of training per week from baseline to follow-up was not different between the two age groups. Age group I trained more than age group II in hours per week both at baseline and follow-up (Table 1).

At follow-up in 2004–2006 age groups I and II had reduced their VO_{2max} from baseline with $19.4 \pm 10.6\%$ and $39.4 \pm 9.0\%$, respectively (Fig. 2). However, both age groups had approximately 170% of normal VO_{2max} among the general healthy male population at the same age. Table 2 shows, in addition, that group I achieved a higher RER than group II and that both groups had a significant decline in VC, FEV_1, HR_{max} and $O_{2\ pulse}$ with ageing. The declines in VO_{2max} (L/min and mL/kg/min), $O_{2\ pulse}$, VC and FEV_1 were significantly greater in group II than in group I. Self-reported 'considerable decrease in training' and competing status were different between the two age groups. Almost half of the subjects in group I reported unchanged training and half of them were still competing in cross-country races, compared with approximately one out of five in the older age group II. Ten in age group I and four in age group II were still competing and reported unchanged training pattern from 1976 to follow-up (Table 3). The number of years of training at the same level before they reduced or stopped training varied among the individuals, with a range from 18 to 51 years in age group I and 14–63 years in age group II.

Eleven subjects in group I reported excellent health, while 20 subjects reported some health problems (data not shown). There was a significant higher VO_{2max} in relative values in mL/kg/min at follow up in those reporting excellent health (52.5 ± 5.8 vs 45.3 ± 8.2, $P = 0.016$), but not in absolute values in L/min (3.8 ± 0.4 vs 3.6 ± 0.7, $P = 0.3$), because of gain of body mass in kilograms among those with health problems (73.6 ± 4.8 vs 79.5 ± 9.2, $P = 0.048$). In group II only six of the 36 subjects reported no health problems. We found no difference in VO_{2max} in relative or absolute values (33.0 ± 5.1 vs 31.2 ± 5.8, $P = 0.60$; 2.6 ± 0.3 vs

Table 1. Age, height, body mass, body mass index (BMI) and training hours per week in two different age groups of Norwegian cross-country skiers at baseline (1976) and follow-up (2004–2006)

Variable	Baseline	Follow-up	Difference 04/06 – 76 (95% CI)	Value *P*
Group I ($n = 32$)	(25–33 years)	(53–62 years)		
Age (years)	29.8 ± 2.1	58.7 ± 2.3	28.9 (29.1, 28.7)	
Height (cm)	179.7 ± 5.9	178.8 ± 6.0	−0.8 (−1.2, −0,5)	0.000
Body mass (kg)	72.4 ± 5.0	77.3 ± 8.3	4.8 (2.5, 7.1)	0.000
BMI (kg/m^2)	22.5 ± 1.6	24.2 ± 2.8	1.8 (1.0, 2.5)	0.000
Training (h/wk)*	7.7 ± 2,0	5.2 ± 2.3	−2.5 (−3.6, −1.4)	0.000
Group II ($n = 36$)	(43–50 years)	(71–79 years)		
Age (years)	46.3 ± 2.4	74.5 ± 2.5	28.1 (28.0, 28.3)	
Height (cm)	178.9 ± 5.3	177.1 ± 4.7	−1.9 (−2.5, −1.3)	0.000
Body mass (kg)	72.8 ± 5.6	75.2 ± 7.3	2.3 (0.4, 4.3)	0.021
BMI (kg/m^2)	22.7 ± 1.4	24.0 ± 2.2	1.2 (0.6, 1.8)	0.000
Training (h/wk)*†	6.1 ± 1.8	4.3 ± 3.2	−1.9 (−2.9, −0.8)	0.001

*Self-reported training time in hours per week

†Data on 33 subjects.

P-values refer to intragroup changes from baseline.

BMI, body mass index.

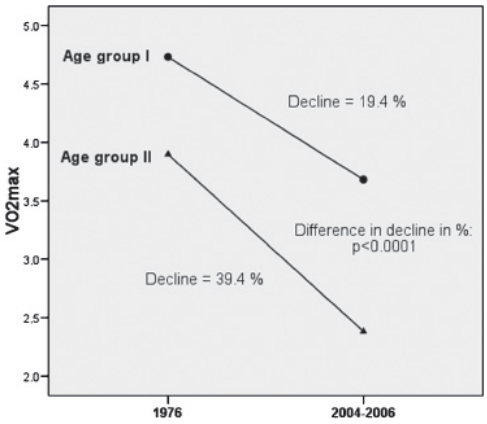

Fig. 2. The decline in VO_{2max} (L/min) from baseline in 1976 to follow-up in 2004–2006 in two different age groups of Norwegian cross-country skiers.

2.3 ± 0.2, $P = 0.12$; respectively) or in body mass (78.8 ± 7.2 vs 74.4 ± 7.3, $P = 0.19$) between 'health' subgroups in group II, but only two out of six men reporting no health problems were still competing.

Two men who had stopped training in group I had both a VO_{2max} at follow-up of 3.2 L/min. They had gained body mass with 10 and 22 kg, respectively. Average VO_{2max} among the six men who had stopped training in age group II was 2.2 ± 0.2 vs 2.4 L/min among the 30 men still training ($P = 0.15$). Gain of weight was 5.8 and 3.0 kg, respectively ($P = 0.22$).

Results among subjects who achieved criteria for VO_{2max}

Table 4 shows data at baseline and follow-up in age groups I and II among those who were still competing and reported unchanged training pattern (UTSC) vs those who had changed either competing status

Table 2. Cardiopulmonary exercise and vitalographic data in two different age groups of Norwegian cross-country skiers at baseline (1976) and follow-up (2004–2006)

Variable	Baseline	Follow-up	Difference 04/06 – 76 (95% CI)	Value *P*
Group I	$n = 32$	$n = 32$		
VO_{2max} (L/min)	4.7 ± 0.5	3.7 ± 0.6	–1.1 (–1.3, –0.8)[¥]	0.000
VO_{2max}, (mL/kg/min)	65.4 ± 5.4	47.8 ± 8.0	– 17.6 (– 20.7, – 14.4)[‡]	0.000
% of normal VO_{2max}		172 ± 27		
RER		1.14 ± 0.06[Φ]		
HR_{max} (beats/min)*	174 ± 11	165 ± 11	– 9.9 (– 14.0, – 5.8)	0.000
$O_{2\ pulse}$[§]	27.4 ± 3.9	22.7 ± 3.3	– 4.5 (– 5.8, – 3.1)[¥]	0.000
VC (L)	5.3 ± 0.6	5.1 ± 0.7	– 0,2 (– 0.3, – 0.1)[†]	0.003
% of normal VC	100 ± 9	114 ± 11	13,3 (10.7, 15.9)	0.000
FEV_1 (L)	4.5 ± 0.5 [‖]	3.9 ± 0.5	– 0,6 (– 0.7, – 0.5)[†]	0.000
% of normal FEV_1	106 ± 11	110 ± 10	4,0 (1.3, 6.7)[†]	0.006
Group II	$n = 36$	$n = 36$		
VO_{2max} (L/min)	3.9 ± 0.4	2.4 ± 0.3	– 1.5 (– 1.4, – 1.6)[¥]	0.000
VO_{2max} (mL/kg/min)	53.8 ± 5.5	31.9 ± 5.4	– 21.8 (– 19.7, – 23.9)[‡]	0.000
% of normal VO_{2max}		168 ± 30		
RER		1.09 ± 0.06[Φ]		
HR_{max}*,[¶] (beats/min)	165 ± 11	151 ± 15	– 14.7 (– 20.7, – 8.7)	0.000
$O_{2\ pulse}$[‖]	23.8 ± 3.0	16.0 ± 2.8	– 7.7 (– 9.0, – 6.4)[¥]	0.000
VC (L)	4.9 ± 0.7	4.2 ± 0.8	– 0.6 (– 0.8, – 0.5)[†]	0.000
% of normal VC	100 ± 11	107 ± 17	6.9 (3.1, 10.7)	0.001
FEV_1 (L)	4.1 ± 0.5**	3.1 ± 0.4	– 1.0 (– 1.1, – 0.8)[†]	0.000
% of normal FEV_1	109 ± 14	102 ± 13	– 7.5 (– 12.3, – 2.8)[†]	0.003

*Excluding those on β-blockers and those with atrial fibrillation during testing.

[§]Data on 30 subjects.

[¶]Data on 29 subjects.

[‖]Data on 31 subjects.

**Data on 33 subjects.

P-values refer to intragroup changes from baseline.

[Φ]$P = 0.002$ between groups at follow-up.

Between groups differences in longitudinal changes:

[¥]$P = 0.001$.

[‡]$P = 0.022$.

[†]$P = 0.0001$.

VO_{2max}, maximum oxygen uptake; RER, respiratory exchange ratio; HR_{max}, maximal heart rate; O_2 pulse, VO_{2max} in mL/min/HR_{max}; VC, vital capacity; FEV_1, one second forced expiratory volume.

Table 3. Self-reported training and competing status in two different age groups of Norwegian cross-country skiers at follow-up (2004–2006)

	Group I ($n = 32$)	Group II ($n = 36$)
Training change		
Unchanged	15	7
Reduced*	15	23
Stopped	2	6
Age reduced or stopped	45.8 ± 9.5	64.1 ± 7.9
Still competing		
Yes	16	6
No	16	30
Age stopped competing	46.9 ± 9.2	63.9 ± 8.3
Still competing and unchanged training	10	4

*Reduced, self-reported 'considerable decrease in training'.

and/or training pattern (CTCS). Those who had stopped training (one in group I and two in group II) are excluded from the statistical analysis. There was a significant difference in the change from baseline to follow-up in VO_{2max}, both in relative values (mL/kg/min) and absolute values (L/min) in group I (but only a tendency in group II) between UTSC and CTCS (Fig. 3).

No difference was found when comparing those in group I who were still competing, but had reduced training time with those who had stopped competing, but had not reduced training time or with those who had both stopped competing and had reduced training time (data not shown). These three different subgroups (together called CTCS) had no significant

Table 4. Subjects' characteristics in two different age groups of 52 'still training' Norwegian cross-country skiers at baseline (1976) and follow-up (2004–2006) according to competing status and their self-reporting training status

Variable	Unchanged training and still competing (UTSC)		Change in training and/or competing status (CTCS)		Difference in change 04/06 − 76 between UTSC and CTCS (95% CI)
	Baseline	Follow-up	Baseline	Follow-up	
Group I	$n = 10$	$n = 10$	$n = 18$	$n = 18$	
VO_{2max} (L/min)	4.7 ± 0.5	4.1 ± 0.6†	4.8 ± 0.4	3.6 ± 0.4†	0.6 (0.2, 0.9)¥
VO_{2max} (mL/kg/min)	65.0 ± 4.7	54.3 ± 6.0†	66.5 ± 4.9	47.7 ± 4.3†	8.1 (2.9, 13.3) ◘
RER		1.15 ± 0.05		1.14 ± 0.06	
HR_{max} (beats/min)	175 ± 9	164 ± 8†	173 ± 11	165 ± 10†	− 3.9 (− 12.5, 4.7)
BM (kg)	72.4 ± 7.1	76.2 ± 6.7†	71.6 ± 3.6	76.1 ± 7.5†	0.7 (− 3.9, 5.3)
VC (L)	5.4 ± 0.4	5.2 ± 0.5	5.3 ± 0.7	5.1 ± 0.7	0.1 (− 0.2, 0.3)
FEV_1 (L)	4.6 ± 0.3	4.0 ± 0.4	4.4 ± 0.5	3.9 ± 0.5	− 0.1 (− 0.3, 0.1)
Age (years)	29.4 ± 2.2	58.3 ± 2.2	29.7 ± 2.2	58.6 ± 2.4	
Time‡	6.7 ± 1.9	6.0 ± 1.6[a]	8.0 ± 2.1	5.6 ± 1.8†	1.7 (0.1, 3.3) ◇
Years§		43.1 ± 3.7		39.1 ± 11.1	
Group II	$n = 4$	$n = 4$	$n = 20$	$n = 20$	
VO_{2max}	4.0 ± 0.3	2.7 ± 0.2†	4.0 ± 0.3	2.3 ± 0.4†	0.3 (− 0.1, 0.7) ○
VO_{2max} (mL/kg/min)	55.9 ± 5.2	38.3 ± 4.2†	54.4 ± 5.5	31.2 ± 5.6†	5.5 (− 1.3, 12.4)•
RER		1.09 ± 0.03		1.11 ± 0.04	
HR_{max} (beats/min)	156 ± 11	157 ± 15	164 ± 9	147 ± 12†	− 16.0 (− 33.7, 1.7)
BM (kg)	72.5 ± 4.2	72.3 ± 9.5	73.4 ± 5.7	75.6 ± 6.9*	0.6 (− 4.3, 5.5)
VC (L)	4.5 ± 0.6	3.9 ± 0.7	5.0 ± 0.6	4.3 ± 0.7	0.1 (− 0.4, 0.6)
FEV_1 (L)	3.8 ± 0.5	2.9 ± 0.5	4.2 ± 0.4	3.1 ± 0.3	0.3 (− 0.1, 0.7)
Age (years)	44.5 ± 1.0	72.5 ± 1.0	46.8 ± 2.3	75.0 ± 2.4	
Time‡	6.5 ± 1.8	5.5 ± 2.9	5.9 ± 2.1	5.0 ± 3.1	− 0.2 (− 3.4, 3.0)
Years§		52.8 ± 7.5		44.5 ± 11.1	

‡Self-reported training time in hours per week.

§SELF-reported hard training in number of years.

Within training groups changes:

†$P < 0.001$.

[a]$P = 0.09$.

*$P < 0.05$.

Between UTSC and CTCS groups' changes:

¥$P = 0.004$.

◘$P = 0.003$.

◇$P < 0.05$.

○$P = 0.13$.

•$P = 0.11$.

VO_{2max}, maximum oxygen uptake; RER, respiratory exchange ratio; HR_{max}, maximum heart rate; VC, vital capacity; FEV_1, one second forced expiratory volume; BM, body mass.

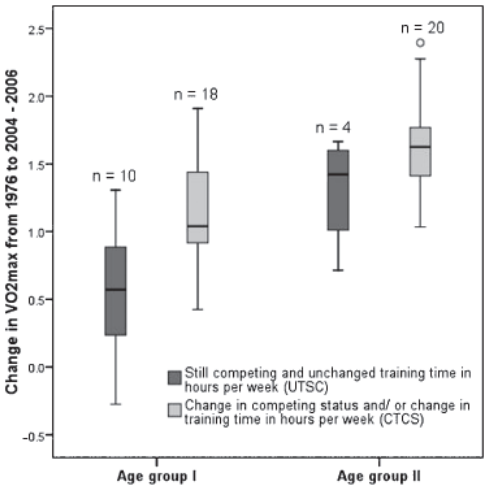

Fig. 3. The change in VO_{2max} (L/min) from baseline in 1976 to follow-up in 2004–2006 in two different age groups of Norwegian cross-country skiers still competing and reporting unchanged training hours per week vs those reporting either change in competing status and/or considerable change in training hours per week.

difference in the decrease in VO_{2max} in L/min/decade (0.40 ± 0.16, 0.37 ± 0.15 and 0.40 ± 0.16, respectively).

A significant difference in change in VO_{2max} was found when comparing still competing men with those who had stopped competing in age group I (0.8 ± 0.6 vs 1.2 ± 0.5; $P = 0.043$), and when comparing those with unchanged training hours per week with those who reported reduced training time in group I (0.7 ± 0.5 vs 1.2 ± 0.4; $P = 0.033$). No change was found for these subgroups in age group II (data not shown).

Table 5 shows data for 28 subjects in group I and 24 subjects in group II, and for UTSC and CTCS in subgroups. As shown the subjects who were still competing and had unchanged training pattern in group I had the lowest decrease in VO_{2max} in L/min/decade and in %/decade.

Correlations

Correlation was found between achieved VO_{2max} (L/min) at baseline and follow-up among all 68 subjects ($r = 0.71$, $P = 0.0001$) and among 55 subjects who reached RER > 1.05 ($r = 0.73$, $P = 0.0001$).

Assessment both at baseline and follow-up showed a significant correlation between VO_{2max} and VC (among 55 subjects who reached RER > 1.05 at follow-up) ($r = 0.50$, $P = 0.0001$ and $r = 0.58$, $P < 0.001$, respectively) and between VO_{2max} and FEV_1 ($r = 0.42$, $P = 0.002$ and $r = 0.75$, $P < 0.001$, respectively). A significant correlation was found between the change in VO_{2max} and the change in VC from baseline to follow-up ($r = 0.43$, $P = 0.001$).

Table 5. Rates of decline in VO_{2max} in 'unchanged training and still competing' (UTSC) vs. 'change in training and/or competing status' (CTCS) in Norwegian cross-country skiers from baseline (1976) to follow-up (2004–2006)

Age group	Decline/decade	Training/competing group	Decline/decade
I $n = 28$		UTSC $n = 10$	$0.19 \pm 0.17^{\dagger}$
	$0.32 \pm 0.18^{*}$		$(4.1 \pm 3.7)^{\ddagger}$
	$(6.7 \pm 3.6)^{*}$	CTCS $n = 18$	$0.39 \pm 0.15^{\dagger}$
			$(8.1 \pm 2.8)^{\ddagger}$
II $n = 24$		UTSC $n = 4$	0.47 ± 0.15^{1}
	$0.55 \pm 0.14^{*}$		$(11.4 \pm 3.2)^{2}$
	$(13.9 \pm 3.2)^{*}$	CTCS $n = 20$	$0.57 \pm 0.13)^{1}$
			$(14.4 \pm 3.0)^{2}$

Results are shown in litre/min per decade and (% decrease per decade).
Between age groups:
$^{*}P = 0.0001$.
Between UTSC and CTCS:
$^{\dagger}P < 0.004$.
$^{\ddagger}P = 0.003$.
$^{1}P = 0.17$.
$^{2}P = 0.09$.

Maximum heart rate correlated with VO_{2max} at follow-up ($r = 0.50$; $P = 0.0001$. At follow-up there was also a significant correlation between training time in hours per week and VO_{2max} ($r = 0.31$, $P = 0.012$). No correlation was found between Δbody weight and ΔVO_{2max} among all subjects ($r = 0.16$, $P = 0.19$). ΔVO_{2max} was significantly correlated to age-adjusted health status ($r = 0.29$, $P = 0.035$ In a multiple regression model (including 55 subjects who reached VO_{2max} at follow-up) Δbody weight, Δtraining time, ΔVC, ΔFEV_1 and health status and competing status at follow-up explain 40% ($P = 0.001$) of the variance of the decline in maximum oxygen uptake with ageing. Only 'still competing' status ($P = 0.007$) had a significant effect in this model. ΔHR_{max} could not be used in this model due to the differences in testing. However, if expected normal values at baseline were added the result would still be the same.

Discussion

The study is unique and to the best of our knowledge, it represents the longest longitudinal study evaluating the effects of aging and competing and training status for as many as 68 subjects from two different age groups with regard to cardiovascular capacity and anthropometric measures among former highly trained men. The material, especially from group I,

where only 3 subjects are missing, is assumed to be highly representative for describing what happens with physiological cardiorespiratory parameters with aging among these subjects. Data from age group II represent 36 out of 48 subjects (75%). The participating subjects were those still alive and with independent living. Still, the data are assumed to be representative for the survivors in this group, because of the 90% recruitment rate.

The major findings are (1) that there was a higher decline in VO_{2max} in L/min per decade and in % per decade in age group II compared with age group I, (2) that the rate of decline in VO_{2max} was lowest among those who reported unchanged training and were still competing in age group I, (3) that nearly all men were in very good physical condition (measured in VO_{2max}) and only eight (12%) out of 68 men had stopped training, (4) that the decline in respiratory function (VC and FEV_1) was one of many possible factors that may explain the decline in VO_{2max}, and that the decline in pulmonary function was higher in age group II than in age group I.

Ageing and cardiovascular function

The present study shows that the decline in maximum oxygen uptake in L/min/decade and in %/decade is higher in age group II than in age group I among the subjects who reached VO_{2max}, Thus, there was a difference in the longitudinal decline in VO_{2max} in ageing from 30 to 59 years compared with ageing from 46 to 75 years indicating a higher decline in VO_{2max} with increasing age. The present data does support the findings in the 'Baltimore Longitudinal Study of Aging' (Fleg et al., 2005) and in the cross-sectional study by Wiswell et al. (2001), where they found an accelerated decline in VO_{2max} with ageing. However, comparison between the age groups in our study must be made with some caution, because of the different ways of assessing VO_{2max} in 1976 and in 2004–2006, as described in 'Materials and methods'.

The decline in VO_{2max}, in this present study, with ≈ 7 and ≈ 14%/decade in age groups I and II, respectively, is not far from results reported by others for age group II, but somewhat lower for age group I (Åstrand et al., 1973; Shvartz & Reibold, 1990; Trappe et al., 1996), but in contrast to the study by Åstrand et al. (1997), where they found a decrease of 23% in VO_{2max} from 1949 to 1970, but no further decrease from 1970 to 1982. Increased training from 1970 among some of the subjects might have contributed.

HR_{max} decreased significantly with ageing in both age groups in our study, as shown by others (Åstrand, 1960; Saltin & Grimby, 1968; Åstrand et al., 1973; Robinson et al., 1976; Tanaka et al., 2001). Decline in the heart's chronotropic response to exercise is responsible for this decrement (Gellish et al., 2007).

In our study, HR_{max} at baseline is lower than expected from the normally used equations (Gellish et al., 2007). Mean expected values in age group I should be over 186 beats per minute (bpm) and in age group II over 174 bpm. Measured values ranged from 12 to 13 beats/min lower than this. The lower HR_{max} at baseline in this population may be due to lower maximum heart rate in endurance-trained than in sedentary men, but more likely due to lower heart rates at maximum exercise on cycle ergometer compared with treadmill (Thompson, 2001, Ref.1). We did not find the same lowered HR_{max} compared with normal values at follow-up among the best-trained and still competing subjects.

$O_{2\ pulse}$ decreased significantly with aging among our subjects. This supports the findings in the studies by McGuire et al. (2001a) and Fleg et al. (2005), indicating that the decline in VO_{2max} occurred because of a reduced maximum stroke volume and/or arterio-venous O_2 difference ($AVDO_{2max}$). In contradiction to these findings Stathokostas et al. (2004) found no change in $O_{2\ pulse}$ 10 years after the initial testing. Spina et al. (1998) found that there is no change in central mechanisms (cardiac output), but that the decline in cardiovascular function with increasing age mainly is due to a decrement in $AVDO_{2max}$. Proctor and Joyner (1997) showed that VO_{2max} per kilogram of limb muscle was reduced in highly trained older men and women compared with highly trained younger subjects. The decline in $O_{2\ pulse}$ was significantly greater in group II than in group I in our study, supporting the finding by Fleg et al. (2005) that the decline in $O_{2\ pulse}$ may not be linear, but increases with increasing age also in a well-trained population. A direct comparison between the two different age groups should, however, be made with caution due to biased HR_{max} and possible variability in VO_{2max} at baseline.

Most of the men had some health problems (most musculo-skeletal). Even if we did not find any significant difference between those with and without reported health problems and the change in VO_{2max} within each age group (data not shown), there was a significant correlation between age-adjusted health status and the decline in VO_{2max}, in the way that those who reported good health had the lowest decrease in VO_{2max} from baseline to follow-up.

Men with health problems had gained more body mass and had a lower VO_{2max} at follow-up than the men reporting excellent health. Health problems are increasing with increasing age in our population, and only six men out of 36 in age group II reported no health problems. It must be assumed that health problems contribute to the accelerated decline in VO_{2max} with ageing.

Ageing and competing/training status

Cross-country skiers in age group I, who were still competing and reported unchanged training time in hours per week had a slower decline in VO_{2max} ($\approx 4\%$/decade) vs those who had either changed competing status and/or training time ($\approx 8\%$ per decade), even if there was no significant difference in number of years with hard training. In the '22-year longitudinal study' among elite distance runners Trappe et al. (1996) found that the high intensity group had a decrease of $\approx 4\%$/decade, while the decrease among master athletes 20 years older, but still training was 14%. In the study by Rogers et al. (1990) there was $\approx 5\%$ decrease per decade among master athletes vs $\approx 13\%$ in the sedentary control group in ageing from ≈ 54 to 62 years. In group II, we did not find the same differences as in group I among subgroups in our study. However, the men who had stopped competing in group II participated in competitions until the age of about 64, and most of them were still training and had a high age-related VO_{2max} at follow-up. We do not know how intensive a 75-year-old man is training, even if he is participating in competitions or reports unchanged training. There were only four subjects still competing and with unchanged training pattern in this group, also indicating risk for statistical type 2 errors. We do not have any data on training intensity or energy expenditure during training. It may be assumed that training intensity is decreasing with increasing age in the higher age groups, so even if the training volume is maintained the effect of training is probably less (Pimentel et al., 2003; McGuire et al., Part II, 2001).

To continue to compete and exercise vigorously, however, attenuated the decrease in VO_{2max} significantly, as shown also in 'the 20-year follow-up study of older track athletes' by Pollock et al. (1997) and in 'the 33-year follow-up study' by Kasch et al. (1999). It must be assumed that participating in competitions will lead to harder and more intensive training generally. In both age groups in this present study, VO_{2max} was significantly higher at follow-up among the still competing and unchanged training subjects, as also shown among still active and former master orienteers (Saltin & Grimby, 1968). In another study of former elite athletes an important decline in VO_{2max} was found, with $\approx 20\%$ the first decade and $\approx 10\%$ the second decade among former Olympic oarsman, who did not continue vigorously training (Hagerman et al., 1996). Katzel et al. (2001) found a decline two to three times as high among former athletes compared with a sedentary control group in a follow-up study after ≈ 9 years. However, still 'intensive training' subjects had no significant decline in VO_{2max} in that study.

It has been discussed if the decline in VO_{2max} is the same in endurance trained as in sedentary men. In our study, we found a lower decline than reported for sedentary men (Inbar et al., 1994) in age group I ($\approx 7\%$ vs 10%), but not in age group II ($\approx 14\%$ vs 15%) (Shvartz & Reibold, 1990). In the meta-analysis by Wilson & Tanaka (2000), consisting of mostly cross-sectional studies, they found the same decline in VO_{2max} in endurance trained as in sedentary men. Pimentel et al. (2003), however, found a greater rate of decline in VO_{2max} with ageing in endurance-trained than in sedentary men in a cross-sectional study.

This present study shows that the annually decline in VO_{2max} cannot be stopped by continued training and competition at a high level in former highly trained men. However, the decline for the subjects in group I with unchanged training and competing patterns shows that it is possible to attenuate the decrease in VO_{2max} by maintaining or increasing exercising, as also showed by Åstrand et al. (1997) and McGuire et al. (2001b). However, the effect of 'still competing and unchanged training pattern' seems to be reduced at older age.

Ageing and respiratory function

In our study, VC decreased with only 7 mL/year in the youngest age group, while FEV1 decreased with 21 mL per year. In age group II, the decrease per year was 25 mL in VC and 36 mL in FEV_1. These data are very close to the values described by Knudson et al. (1976) and Janssens (2005), indicating an accelerated decline in pulmonary function with ageing Both age groups have normal values of VC and FEV1 both at baseline and follow-up.

It is not thought that a decline in VC and FEV_1 are responsible for some of the decline in VO_{2max} with aging (Thompson, 2001 Ref. 2). In our study, there was a significant correlation between the change in VO_{2max} and the change in VC from baseline to follow-up among those who performed a maximum test. We also found a significant correlation between VC and VO_{2max} among the same 55 subjects both at baseline and follow-up. In the literature, it is reported that gas exchange is well preserved at rest and during exertion in the older male (Janssens et al., 1999), assuming that the reduction in pulmonary function is not an independent responsible factor for the reduction in VO_{2max} with aging.

Study limitations

The present study has some limitations. It illustrates a major limitation in long time longitudinal studies, where different techniques in assessing parameters

(here VO_{2max}) between baseline and follow-up have been used. This could lead to some variability, as described in 'Materials and methods'. Respiratory function was also assessed with two different methods, but the results seem to be within normal ranges both at baseline and follow-up. The study did not have any sedentary control group from baseline until the present, which could disclose any confounding variables between these highly trained males and other endurance trained or sedentary men.

The study was uncontrolled with regard to training volume and intensity, but was based upon self-reported training time in hours per week. However, it was controlled with regard to 'still competing' or not in the official result lists.

We do not have data on fat-free body mass, which could say something about loss of muscle mass with ageing as a possible explanation for the higher decline in VO_{2max} in age group II than in age group I.

Some of the results could be biased, because of small numbers of subjects in subgroups.

Perspectives

We conclude that the age related decline in cardiovascular capacity is not far from results reported in other studies for still endurance trained men and healthy men from the general population for age group II, but somewhat lower for age group I. Decline in VO_{2max} is greater in age group II compared with age group I. Men in age group I, but not in age group II, with unchanged training patterns and who were still competing experienced a significant attenuated decrease in the longitudinal decline in VO_{2max} compared with the others. Still, this study shows that lifelong active and highly endurance trained men cannot stop the decline in VO_{2max} with advancing age However, both men in group I and II have a VO_{2max} high above the age-related expected values for VO_{2max} at follow-up. Training and competing are the most important factors to maintain a high level of VO_{2max} with ageing.

Key words: ageing, longitudinal, maximum oxygen uptake, training, competing.

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Echocardiographic evaluation of aged male cross country skiers

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The aim of this echocardiographic study was to evaluate the effects of long-term endurance training on cardiac structure and function in three different age groups of 48 healthy middle-aged and old former or still active male cross country skiers (23 in age group I: age 58.6 ± 2.2 years; 21 in age group II: age 74.9 ± 2.2 years; four in age group III: age 89.5 ± 1.9 years). The two oldest age groups were combined and compared with age group I. No significant differences in left atrial or ventricular dimensions between these two age groups were found. A high proportion of enlarged left atrial dimensions were found among all subjects with 80% exceeding the upper reference limit of 40 mm in diameter (LADs) and 94% exceeding the upper reference limit of 20 cm^2 in area (LAAs). Mean values for LADs (mm) and LAAs (cm^2) were: group I: 41.9 ± 4.7 and 24.7 ± 3.3; group II: 43.5 ± 4.8 and 25.2 ± 3.7; group III: 44.5 ± 4.7 and 25.8 ± 3.7. Left ventricular diastolic diameter exceeded the upper reference limits of > 54 mm in 20 subjects among all. The groups had preserved systolic and age-related diastolic function.

Long-term endurance training leads to improved performance due to enhancements in cardiac output (CO), muscle oxidative capacity and improved mechanical efficiency (Maron & Pelliccia, 2006; Holmberg et al., 2007; Levine, 2008). Maximal cardiac output (CO_{max}) is the single most important factor that limits maximal oxygen uptake (VO_{2max}) in healthy subjects (Saltin, 1985). Long-term physical training is associated with cardiac morphological changes called the athlete's heart (Maron, 1986; Spirito et al., 1994; Sharma, 2003). For cross country skiers, as for other endurance athletes, the adaptive changes include increased left and right ventricular and left atrial cavity size and volume, and to a lesser degree left ventricular eccentric hypertrophy; these changes are found to be associated with normal diastolic and systolic function (Pelliccia et al., 1999; Maron & Pelliccia, 2006).

On cellular level, physical training leads to faster rise and decay in intracellular calcium transient in cardiomyocytes and improved myofilament sensitivity to calcium, which in turn results in improved cardiac contractile function (Wisløff et al., 2009).

VO_{2max}, maximal heart rate (HR_{max}) and CO_{max} decrease with age in master athletes as in the general population (Åstrand, 1960; Saltin & Grimby, 1968; Wilson & Tanaka, 2000; Fleg et al., 2005; Grimsmo et al., 2009). The reduction in cardiac function with aging occurs mostly because of decreased cathecolamine sensitivity, prolongation of excitation–contraction and IVRTs, increased afterload and increased vascular and myocardial stiffness (Douglas & O'Toole, 1992; Spina et al., 1998). Age-related echocardiographic findings in healthy older people include increased left ventricular wall thickness without dilatation or concentric hypertrophy, prolonged IVRT and reduced diastolic function (Gates et al., 2003; Lakatta & Levy, 2003; Masugata et al., 2007). Data on echocardiographic findings in the old athlete are limited and there are diverging results in the literature on whether long-term endurance training leads to irreversible changes later in life, such as left atrial enlargement and/or ventricular enlargement and hypertrophy leading to morbidity (Baldesberger et al., 2008; Luthi et al., 2008; Attenhofer Jost & Jenni, 2009; Bjørnstad et al., 2009).

The purpose of the present study was to evaluate the effects of long-term endurance training on cardiac structure and function in three different age groups of middle-aged and older former or current male cross country skiers without cardiovascular or pulmonary diseases.

Material and methods

Study population

In 1976, Lie and Erikssen (1978) examined 122 skiers in three preselected age groups, who for many years had been among the

best quartile in different endurance cross country competitions. All of the men were recruited from the 58-km-long Norwegian "Birkebeiner" cross country race and they had obtained "the Birkebeiner medal" several times (among the best quartile in each age group). The material and criteria for entering the study are described in detail elsewhere (Lie & Erikssen, 1978; Grimsmo et al., 2009). All men still alive from the original population were asked to participate in a follow-up study. The Norwegian Regional Ethical Committee approved the study protocol, after exclusion of the oldest age group III from exercise testing. Permission was given from the Norwegian Data Inspectorate and the Norwegian Board of Health. All of the participants provided informed consent to the approved study protocol.

Out of the original 122 subjects, 37 (30%) had died during the period from 1976 to 2006, with 1/35 in group I, 8/48 in group II and 28/39 in group III. One in group I was not found in the central Norwegian population register. Three from group II and three from group III did not respond to the invitation. Thus, 78 subjects participated in the follow-up study from 2004 to 2006 (33 in group I: age 54–62 years; 37 in group II: age 72–79 years; and eight in group III: age 88–92 years).

In this present study, we included 48 healthy lifelong master athletes with 23 in age group I, 21 in age group II and four in age group III. All subjects with cardiac and/or pulmonary diseases and subjects on cardio active medication, which could interfere with the echocardiographic findings, were excluded (10 subjects from group I, 16 from group II and four from group III with atrial fibrillation, coronary heart disease, congestive heart failure and/or hypertension).

Questionnaires

The subjects answered questions about lifelong training and competition patterns and history, identical to the questions answered in the two earlier studies (Lie & Erikssen, 1978, 1984). In addition, they answered questions about medical status and detailed questions about heart and lung diseases.

Physical examination and exercise testing

The examination program included a physical status, a vitalographic assessment and a maximal treadmill exercise test with ECG (except the four subjects in group III) (Grimsmo et al., 2009). Resting ECG was taken before the start of the exercise test in groups I and II and before the echocardiography in group III. The maximal exercise test was performed on a "Woodway" treadmill (Marquette Electronics Case 15, Milwaukee, Wisconsin, USA), according to the modified Bruce protocol (Bruce, 1978). Metabolic and respiratory parameters were measured using a Sensor Medics Vmax 29 C-2130 Spirometer (Sensor medics Corp., Yourba Linda, California, USA). The exercise test was supervised by one investigator (J. G.) following the guidelines of the European Society of Cardiology (ESC Working Group, 1993).

Echocardiography

Complete two-dimensional, M-mode and Doppler recordings at rest were obtained with a VingMed Vivid 7 (Vingmed Sound, Horten, Norway) echocardiograph. All recordings were obtained by one study investigator (I. G.), using standard methods of measurements (Lang et al., 2005; Grundvold et al., 2008).

Statistical analysis

Data analysis was performed with the statistical package for the social sciences version 16, 2008. The data were tested for normal distribution using quintile–quintile plots. Differences between mean values were assessed with the unpaired Student's *t*-test and differences of proportions were assessed by the chi-square test. A two-tailed P value <0.05 was considered significant. Results are expressed as mean ± SD. Age-adjusted correlations or linear regression analyses were used to assess associations between different parameters. Age group III is combined with age group II in the statistical assessments, due to the limited number of subjects.

Results

Cardiovascular capacity, training/competing patterns and age

Table 1 shows that age group I had lower resting systolic blood pressure (SBP) than age group II and age groups II and III combined, whereas no difference between age groups was found for resting diastolic blood pressure or resting heart rate. Age group I had higher maximal SBP, HR_{max} and VO_{2max} but lower diastolic blood pressure at maximal treadmill testing than age group II.

Table 1 also shows the number of years of hard training before self-reporting considerable decrease in training time and/or intensity in the three different age groups. Number of years of hard training ranged from 18 to 63 among all participants. Eight subjects had lifelong hard training for <30 years; whereas 13 had >50 years (data not shown). Even if the result in Table 1 only shows a tendency to a reduced training time in hours per week between the youngest age group I and the combined older groups (II and III), we found a significant correlation between reduced training time and increased age in a bivariate regression analysis model ($r = 0.31$, $P = 0.038$).

Echocardiographic findings and age

Table 2 shows that there was no difference between younger and older age groups for end-diastolic left ventricular diameter (LVDd), anterior ventricular septal (IVSd) and posterior free wall thicknesses (LVPWd) or left atrial dimensions in ventricular systole (LADs and LAAs). Totally, 28 subjects among all had LVDd less than the upper reference limit of 55 mm (Pelliccia et al., 1999; Sharma, 2003), 14 had dimensions between 55 and 59 mm and six had dimensions ≥ 60 mm (three in age group I, two in age group II and one in age group III, respectively). No one had IVSd or LVPWd exceeding the upper reference limits of >12 mm (Sharma, 2003). Eight subjects had LADs less than upper reference limit of <40 mm (Pelliccia et al., 2005), 21 had LADs between 40 and 45 mm, whereas 18 had diameter ≥ 45 mm (including three with a diameter ≥ 50 mm). LAAs was within normal reference limits of $\leq 20\,cm^2$ (Lang et al., 2005) in only three subjects, while 38 had areas between 21 and $30\,cm^2$ and seven had an area $\geq 30\,cm^2$. Figure 1(a),

Table 1. Demographic, some clinical and training/competing data in three different age groups of 48 male long-term endurance cross country skiers

Age group numbers (n)	Group I ($n = 23$)	Group II ($n = 21$)	P-value (I vs II)	Group III ($n = 4$)	P-value (I vs II+III)
Age (years)	58.6 ± 2.2	74.9 ± 2.2	0.000	89.5 ± 1.9	0.000
Range age (years)	(54–62)	(72–79)		(88–92)	
Height (cm)	178.5 ± 6.0	178.3 ± 3.8	NS	163.8 ± 7.5	NS
Body mass (kg)	76.0 ± 7.4	75.8 ± 7.7	NS	67.3 ± 5.7	NS
BMI (kg/m^2)	24.0 ± 3.1	23.9 ± 2.1	NS	25.3 ± 3.0	NS
HR rest (beats/min)	56.2 ± 9.4	58.7 ± 7.6	NS	58.8 ± 8.0	NS
HR_{max} (beats/min)	165 ± 9	150 ± 11	0.000		
SBP rest (mmHg)	115 ± 9	125 ± 10	0.001	139 ± 23	0.001
DBP rest (mmHg)	71 ± 8	74 ± 7	NS	73 ± 10	NS
SBP_{max} (mmHg)	188 ± 13	177 ± 16	0.014		
DBP_{max} (mmHg)	65 ± 4	72 ± 7	0.000		
VO_{2max} (litre/min)	3.7 ± 0.5	2.5 ± 0.3	0.000		
Hard train (years)	39 ± 10	46 ± 12*	0.039	54 ± 8	0.010
Acc train (h)	14011 ± 5293	14777 ± 5531*	NS	16468 ± 4036	NS
Train now (h/week)	5.3 ± 2.0	4.2 ± 3.0†	NS	2.5 ± 4.4	NS
HI train (h/week)	1.1 ± 1.1	1.4 ± 1.3‡	NS	0	NS
Age last race (years)	53.5 ± 8.9	66.6 ± 8.5	0.000	78.0 ± 9.5	0.000
Age last medal (years)	51.0 ± 10.2	65.6 ± 8.0	0.000	78.0 ± 9.5	0.000
Number of 'medals'	20 ± 11	24 ± 9	NS	34 ± 10	NS
Stopped train (n)	1	3	NS	3	NS
Red train (n)	14	16	NS	4	NS
Stop comp (n)	10	15	NS	4	NS

*Twenty subjects.

†Eighteen subjects.

‡Nineteen subjects.

BMI, body mass index; HR, heart rate; rest, at rest; min, minutes; SBP, systolic blood pressure; DBP, diastolic blood pressure; max, at maximal exercise; V_{02}, oxygen uptake; train, physical training; Acc train, lifte-long accumulated training hours; medal, among the 25% best (in the same age group) in the Norwegian 54 km cross country ski race "Birkebeiner"; NS, not significant; Red train, subjects reduced training pattern; Stop comp, subjects stopped competing.

Table 2. Echocardiographic variables of left ventricular dimension, left atrial dimensions, systolic and diastolic function and aortic valve velocity in three different age groups of 48 male long-term endurance cross country skiers

Age group	Group I ($n = 23$)	Group II ($n = 21$)	P-value (I vs II)	Group III ($n = 4$)	P-value (I vs II+III)
LVDd (mm)	54.0 ± 0.4	53.0 ± 0.4	NS	53.0 ± 0.7	NS
IVSd (mm)	10.3 ± 1.1	10.1 ± 1.3	NS	10.5 ± 1.7	NS
LVPWd (mm)	10.0 ± 0.7	9.6 ± 1.2	NS	10.0 ± 0.8	NS
LADs (mm)	41.9 ± 4.7	43.5 ± 4.8	NS	44.5 ± 4.7	NS
LAAs (cm^2)	24.7 ± 3.3	25.2 ± 3.7	NS	25.8 ± 3.7	NS
LVEF (%)	60.5 ± 6.0	57.6 ± 5.0	NS	59.2 ± 3.3	NS
SV (mL/beat)	92.7 ± 17.5	79.1 ± 12.4	0.005	70.3 ± 11.9	0.001
E peak velocity (m/s)	0.71 ± 0.14	0.71 ± 0.15	NS	0.78 ± 0.17	NS
E deceleration time (ms)	229 ± 29	273 ± 90	0.03	315 ± 83	0.01
E/A ratio	1.4 ± 0.4	0.9 ± 0.2	0.0001	0.8 ± 0.3	0.0001
IVRT (ms)	108 ± 13*	120 ± 25†	NS	134 ± 6‡	0.03
Aortic valve (m/s)	1.26 ± 0.17†	1.41 ± 0.42	NS	1.68 ± 0.82	NS

*Twenty subjects.

†Nineteen subjects.

‡Three subjects.

d, diastolic; s, systolic; LVD, left ventricular diameter; IVS, interventricular septum; LVPW, left ventricular posterior wall; LAD, left atrial diamter; LAA, left atrial area; LVEF, left ventricular ejection fraction; SV, stroke volum; E, early diastolic; E/A ratio, ratio of the early to late diastolic peak-flow velocities; IVRT, isovolumic relaxation time.

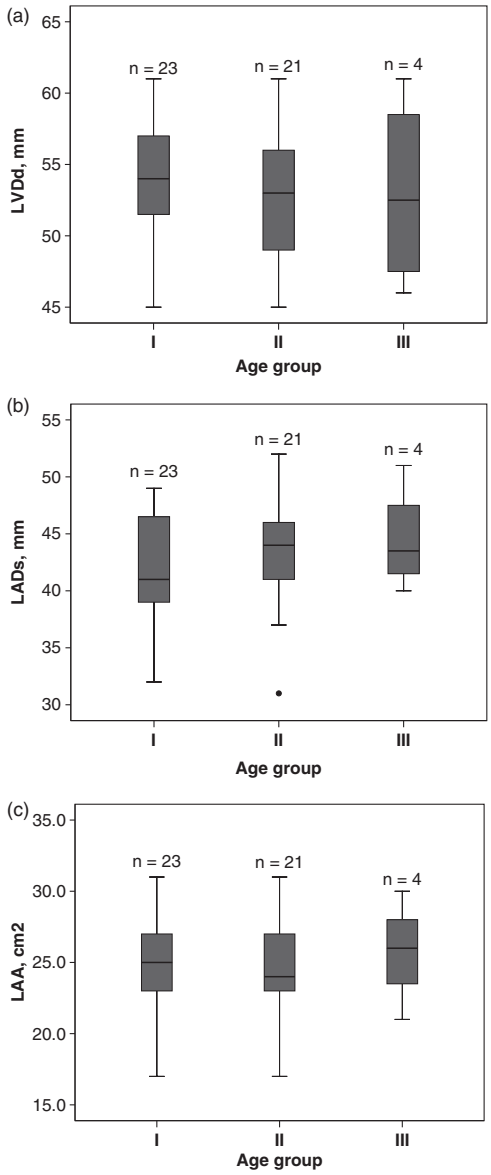

Fig. 1. Left ventricular diameter (LVDd) (a), left atrial diameter (LADs) (b) or left atrial area (LAAs) (c) in age groups I, II and III.

(b) and (c) show left cardiac dimensions (LADs, LAAs and LVDd, respectively) in the three different age groups.

We found a correlation between LVDd and maximum systolic blood pressure (SBP_{max}) in age groups I and II together ($r = 0.30$, $P = 0.048$), also when adjusting for age ($r = 0.26$, $P = 0.048$). Correlations were also found between LVDd and IVSd ($r = 0.32$, $P = 0.025$) and LVPWd ($r = 0.46$, $P = 0.001$), respectively, among all 48 subjects. No correlation was found between age and atrial dimensions (LADs: $r = 0.18$, $P = 0.23$ and LAAs: $r = 0.05$, $P = 0.76$), but LADs was correlated to LVDd ($r = 0.28$, $P = 0.05$) and to LAAs ($r = 0.39$, $P = 0.007$). No correlation was found between body height (cm) and LADs ($r = -0.15$, $P = 0.30$ or LAAs ($r = -0.17$, $P = 0.28$) or body mass index (kg/body height in meter^2) and LADs ($r = 0.26$, $P = 0.07$) or LAAs ($r = 0.08$, $P = 0.61$), respectively.

Diastolic function decreased with increasing age (Table 2). Correlation was found between HR at rest and the ratio of the early to late diastolic peak flow velocities (E/A ratio) adjusted for age ($r = 0.38$, $P = 0.009$). A correlation (adjusting for HR at rest) was also found between age and E deceleration time ($r = 0.43$, $P = 0.002$), E/A ratio ($r = 0.70$, $P = 0.0001$) and IVRT ($r = 0.38$, $P = 0.013$), respectively. Only age was significantly correlated to E/A in a multiple regression model ($P = 0.002$).

All three age groups had normal left ventricular systolic function as expressed in an ejection fraction, and there was no difference between age groups (Table 2). Finally, Table 2 shows that stroke volume calculated at rest decreased significantly with increasing age.

We found mild mitral valve regurgitation in 22 subjects of 44 examined, with 8 of 23 in age group I, 12 of 18 in age group II and 1 of 3 in age group III (data not shown). Aortic valve velocities were increasing with age, although no differences between groups were found (Table 2).

Echocardiographic findings and training/competing status

There was no correlation between different cardiac dimensions (LADs, LAAs, LVDd, IVSd or LVPWd) and different training and/or competing parameters from Table 1 (hard training in numbers of years, lifelong accumulated training hours, present amount of training hours per week, present amount of hours with high-intensity training per week, age when competing for the last time among the upper quartile in the ''Birkebeiner'' race, age when training was reduced or they stopped competing, respectively – data not shown). There was no difference in atrial dimensions (LADs or LAAs, respectively), between those who had or had not stopped competing, or between those who had or had not reduced training time in hours per week among all subjects (data not shown). However, a significant correlation was found between LAAs and numbers among the upper quartile in the ''Birkebeiner'' race ($r = 0.31$, $P = 0.031$).

Discussion

To the best of our knowledge, the present echocardiographic study includes the oldest and largest study population of master athletes yet reported, with 25 healthy former and current long-term endurance-trained cross country skiers with a mean age of 77.2 ± 5.9 years (groups II and III combined including four subjects between 88 and 92 years) compared with an age group of 23 comparable athletes almost 20 years younger.

The major new findings from this present study are (1) that there was a very high proportion of enlarged left atrial dimensions among all, and (2) that no differences in left cardiac dimensions (LADs, LAAs and LVDd, respectively) between the two oldest age groups compared with a younger group of long-term endurance cross country skiers were found.

Only about 40% of the original study group was included, with only four out of 39 in the oldest group remaining. Comparisons between age groups must, therefore, be interpreted with caution in this study. The results may not be representative for the original study population, but they are representative for the healthy survivors (Lazarus & Harridge, 2007). Obvious genetic endowments in the oldest cross country skiers with lifelong participation in endurance training naturally lead to more years of training but on the other hand also lead to reduced training and competition patterns with ageing (Grimsmo et al., 2009).

We found that cardiac adaptive changes due to long-term endurance training in cross country skiers consisted of enlarged left atrial dimensions (LADs and LAAs) and also to a lesser degree, increased LVDd at upper reference limits (Pelliccia et al., 1999). The latter is in accordance with studies in younger cross country skiers and other endurance athletes mostly between 18 and 39 years old (Maron, 1986; Spirito et al., 1994; Pluim et al., 1999; Sharma, 2003; Bjørnstad et al., 2009). Left ventricular wall thickness (IVSd and LVPWd, respectively) also showed dimensions within normal limits similar to younger endurance-trained subjects described in the meta-analysis by Pluim et al. (1999). The correlation between LVDd and wall thickness shows eccentric left ventricular hypertrophy (LVH) in our older groups of cross country skiers as shown among younger cross country skiers and other endurance athletes (Pelliccia et al., 1999). However, our findings with regard to the older athletes were in contrast to the findings in the study by Hood and Northcote (1999), who found that $>50\%$ of veteran runners aged 67 ± 6 years (range 56–83 years) had LVH defined as IVSd and LVPWd in excess of 12 mm. This difference in cardiac adaptation (wall thickness and chamber size) between older cross country skiers and long-distance runners is not verified by others and is in contrast to a study by Fagard et al. (1984) in younger runners compared with bicyclists. Both long-distance running and cross country skiing are mostly dynamic exercises, and much of the same cardiac adaptations to training in these groups should have been expected. In top-level bicycling, an exercise containing both dynamic and static demands, both ventricular hypertrophy and dilatation should be expected as observed in younger cyclists (Fagard et al., 1984; Pelliccia et al., 1999; Hoogsten et al., 2003). However, in two recently published studies among 62 former professional cyclists aged 66 ± 7 years left atrial and ventricular dilatation was found but no ventricular hypertrophy (Baldesberger et al., 2008; Luthi et al., 2008).

Another aspect to be considered is that cross country skiers are among the athletes with the highest measured VO_{2max} (Åstrand et al., 2003; Levine, 2008) because of whole-body exercise (upper and lower body muscles) involved in diagonal skiing (Holmberg et al., 2007). Larger cardiac dimensions and CO_{max} is, therefore, expected among cross country skiers compared with bicyclists and runners, where mostly lower body muscles are involved (Holmberg et al., 2007). The top elite cross country skiers (aged 27.1 ± 3.4 years) in the study by Holmberg et al. (2007) had a VO_{2max} of $\approx 200\%$ of normal age-related values, but the older skiers in our study also had a very high VO_{2max} of 175% of age-related values among all and 185% among the 19 subjects still competing (data not shown). Even if we do not have data on high-intensity training (but only training time in hours per week) from the study in 1976 to follow-up after 28–30 years, we do assume that these skiers are endurance athletes who have trained at high intensities, judging from the data of % of normal VO_{2max} (Wisløff et al., 2009).

We found a correlation between LVDd (at rest) and SBP_{max}. To the best of our knowledge, this correlation has not yet been described in the literature by others. Resting SBP increases with increasing age and maximal SBP decreases with increasing age both among sedentary people and endurance-trained athletes (Vaitkevicius et al., 1993). Endurance training attenuates the increase in resting SBP and the decrease in maximal SBP with aging, because of reduced arterial stiffness in the endurance trained (Vaitkevicius et al., 1993; Levine, 2008). The review by Levine (2008) states that "the large LV filling and ejection allows preservation of blood pressure during extraordinary rates of muscle blood flow and oxygen transport, which support high rates of sustained oxidative metabolism." Even if our data must be interpreted with caution because of small sample sizes, the data indicate that the still healthy older cross country skiers with large left ventricular volume also have the best preserved increase in SBP during exercise because of large blood volume and preserved cardiac

function and arterial compliance. However, this finding has to be confirmed in other studies.

Atrial remodelling due to physical activity in middle-aged and older athletes above 60 years has been described only in two studies (Höglund, 1986; Luthi et al., 2008), but normal atrial dimensions in master athletes are described by others (Bouvier et al., 2001; Baldi et al., 2003). Pelliccia et al. (2005) found that left atrial remodelling with increased left atrial transverse dimensions was present in approximately 20% of highly trained young athletes. Höglund (1986) found left atrial dilatation among 13 former elite endurance athletes with a mean age of 66 years compared with controls, while Bjørnstad et al. (2009) in a 15-year follow-up study they only found mild left atrial dilatation among 15 former top-level athletes in different sports aged approximately 40 years. Thus, in this present study of cross country skiers, we have found one of the highest proportions of enlarged atrial dimensions yet described, with LADs and LAAs exceeding upper normal limits by $>80\%$ and 90%, respectively. The findings could not be explained by other factors, such as mitral regurgitation, hypertension, height or body mass in our population. There was no difference in LADs between those with and without mild mitral regurgitation, and there was no correlation between LADs and blood pressure, height or body mass, respectively (data not shown). Further studies are needed to investigate if these enlarged left atrial dimensions are present in different long-term older athletes and if they are predisposed for morbidity, such as atrial fibrillation (Elousa et al., 2006; Grimsmo et al., 2007; Baldesberger et al., 2008).

The findings in this present study provide evidence that the volume overload (increased preload) and high CO needed during cross country skiing leads to cardiac remodelling with enlarged LADs, which remain at older ages. Hoogsten et al. (2003) found that cardiac remodelling (left atrial and left ventricular dilatation and increased left ventricular mass) already had started in 17-year-old competitive bicyclists compared with controls, and that remodelling was further increased in a group of 29-year-old professional cyclists. Luthi et al. (2008) found that the extent of previous cycling correlated to atrial size after long-term deconditioning in former professional cyclists and that there was an incomplete reverse cardiac remodelling. Still, we do not know when remodelling has possibly reached its maximum and to what extent it is later reversed after detraining at older ages in different groups of long-term endurance athletes.

We found a high proportion of physiological to mild mitral valve regurgitation (50%) in this present study. However, this proportion is somewhat lower than the described for younger athletes in the study by Douglas et al. (1989), where they found that as many as 69% had mild mitral regurgitation vs 29% among control subjects. However, comparison with other studies must be interpreted with caution because of possible differences on definitions of grades, different equipment with different sensibility and different operators. Mild valvular regurgitation in athletes should not have negative physiological consequences but would be another cardiac adaptation to physical training (Thomas & Douglas, 2001).

A strong correlation was found between age and LV diastolic function (E deceleration time, E/A and IVRT, respectively), which is in accordance with other studies (Douglas & O'Toole, 1992). Seals et al. (1994) have shown enhanced systolic function in endurance-trained older men compared with sedentary men, and Arbab-Zadeh et al. (2004) have shown that prolonged, sustained endurance training preserves ventricular compliance, and consequently diastolic and systolic function with aging. Bouvier et al. (2001) have found superior diastolic and systolic function among ten elderly endurance athletes between ages 70 and 80 years compared with controls. In contrary to this, Luthi et al. (2008) have found diastolic dysfunction among former professional bicyclists as assessed by tissue Doppler imaging. Both systolic function expressed in resting LVEF % and age-related diastolic function were normal and preserved with aging among the current and former cross country skiers in the present study.

The present study has some limitations. This cross-sectional study compared two different age-groups of former or current long-term endurance cross country skiers, but a long-term longitudinal study with repeated echocardiographic measurements would have been preferable to comment on the effect of detraining or increased training at older ages on cardiac remodelling. Many of the comparisons in this study are based on determined norms because no control group was present. The number of participants was low with just four subjects in the oldest age group III. We have combined groups II and III to reduce statistical errors. Age group III was too small to be analyzed as a separate group, which would have been of great interest because of lack of studies in the very old former athletes. Unfortunately, the study groups were too small to analyze the effect of detraining separately on cardiac dimensions and function within each age group. Another limitation is that echocardiographic measurements of normal left chamber sizes in the general healthy older male Norwegian population are scarce. We do not have data on left atrial volume index, which is the preferable measurement of atrial size today (Abhayaratna et al., 2006).

Perspectives

In conclusion, we have found that healthy long-term master cross country skiers have enlarged left atrial

dimensions. There was no difference in dimensions between an age group of ≈ 59 years and an age group almost 20 years older. All groups had preserved systolic and age-related diastolic function.

Myocardial fibrosis and less myocardial elasticity have been found in veteran athletes with LVH compared with normal sedentary subjects (Lindsay & Dunn, 2007). Although it is not yet proved, it may be assumed that the same changes with fibrosis are present in a group of middle-aged and old long-term endurance cross country skiers with enlarged left cardiac dimensions. Unchanged dimensions at older ages, when reduced training time and intensity is expected (Pimentel et al., 2003), could at least partly be due to myocardial fibrosis and less elasticity. The consequences of enlarged left atrial dimensions in athletes are still not known (Pelliccia et al., 2005), but increased incidence of atrial fibrillation might be expected, as supposed in the reviews by La Gerche et al. (2009) and Mont et al. (2009). Still, the older cross country skiers in this present study have a cardiorespiratory function, and thus CO high above the expected normal age-related values.

Key words: athlete's heart, aging, long-term endurance sports.

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III

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EUROPEAN SOCIETY OF CARDIOLOGY®

Original Scientific Paper

High prevalence of atrial fibrillation in long-term endurance cross-country skiers: echocardiographic findings and possible predictors – a 28–30 years follow-up study

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Background **Lone atrial fibrillation (LAF) seems to be more common in endurance-trained male athletes than in men in the general population. The reason for this has not been found.**

Aim **To determine the prevalence of LAF in long-term endurance cross-country skiers and to examine possible predictors.**

Methods **Of 149 healthy, long-term trained cross-country skiers from three different age groups who were invited, 122 and 117 participated in the studies in 1976 and 1981, respectively. At follow-up in 2004–2006, 78 men participated, with 33 in age group I (54–62 years), 37 in group II (72–80 years) and eight in group III (87–92 years), whereas 37 individuals had died and seven could not be tracked. The examination programme applied in 1976, 1981 and 2004–2006 consisted of an electrocardiographic monitoring during rest and exercise and a maximal exercise test. Echocardiography was performed in 2004–2006.**

Results **A high prevalence (12.8%) of LAF was found. The only predictor from both 1976 and 1981 associated with LAF was a long PQ time ($r=0.38$, $P=0.001$ and $r=0.27$, $P=0.02$, respectively), whereas bradycardia was another predictor from 1981 ($r=0.29$, $P=0.012$). At follow-up, left atrial enlargement was a marker associated with LAF ($P<0.001$).**

Conclusion **Long PQ time, bradycardia and left atrial enlargement seem to be important risk factors for LAF among long-term endurance cross-country skiers. *Eur J Cardiovasc Prev Rehabil* 17:100–105 © 2010 The European Society of Cardiology**

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Keywords: endurance sports, lone atrial fibrillation, predictors, prevalence

Introduction

Lone atrial fibrillation (LAF) is supposed to be more common in long-term endurance-trained male athletes than in the general male population [1–5]. The prevalence of atrial fibrillation (AF) among men younger than 40 years of age in the general population is as low as 0.5% and increases up to more than 15% in men who are 75 years or older [6,7]. The prevalence of LAF in different studies varies from 2 to 50% dependent on the chosen study population with AF [8,9].

Only a few investigators have suggested possible predictors for the assumed increased prevalence of LAF among endurance-trained athletes [5,10,11]. Such predictors remain speculative and include atrial ectopic beats, inflammatory changes, changes in electrolytes, atrial enlargement with dilatation and fibrosis and increased vagal tone and bradycardia [12–14]. In cross-country skiers, cardiac adaptation to physical training includes increased left and right ventricular and left atrial cavity size and volume and to a lesser degree left ventricular hypertrophy (LVH) [15]. Atrial remodelling with increased left atrial dimensions because of long-term physical activity has been reported in young athletes [16] and middle-aged and older athletes (> 50 years) [17]. Left atrial enlargement is an independent predictor of AF in the general population and in patients with structural heart disease [16,18].

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Part of this study was previously presented in abstract form at the Europrevent 2007, Madrid, Spain [*Eur J Cardiovasc Rehabil* 2007; 14 (Suppl 1)] and ESC Annual Congress 2007, Vienna, Austria [*Eur Heart J* 2007; 28 (Suppl 1):P645].

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The aim of this follow-up study was to (i) determine the prevalence of AF and LAF among former healthy cross-country skiers studied for the first time in 1976, (ii) examine possible predictors for the development of LAF and (iii) assess if any differences were present in echocardiographic findings at follow-up between those with and without LAF.

Population and methods

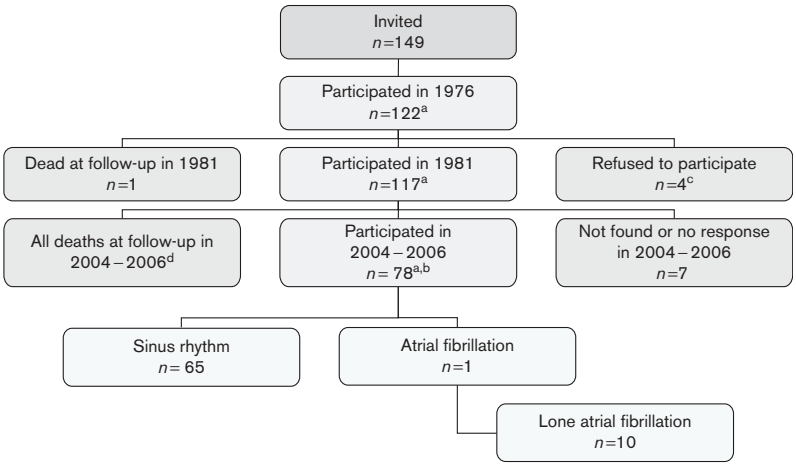
Cross-country skiers in three preselected age groups, who competed in the Norwegian 'Birkebeiner' race of 58 km, were invited to participate in the study. Of the 149 invited skiers, 122 participated in the first study in 1976, with 35 from group I (age 26–33 years), 48 from group II (age 43–50 years) and 39 from group III (age 58–64 years). The inclusion criteria were that they (i) for several years had participated in long-distance (30–90 km) cross-country competitions, and (ii) in general were among the one-quarter of individuals with the best age-related performance in the various contests [19]. Of the 122 skiers, 117 participated in a 5-year follow-up study in 1981 [20].

All of the men still alive from the original population were asked to participate in this follow-up study in 2004–2006. The Norwegian Regional Ethics Committee approved the study protocol, after exclusion of the oldest age individuals (i.e. those in group III) from exercise testing. Permission was given from the Norwegian Data Inspectorate and the Norwegian Board of Health. All of the participants provided informed consent to the approved study protocol. Of the original 122 participants, 37 had died before 2006, with one in group I, eight in group II and 28 in group III. One in group I was not found in the central Norwegian Population Register. Three from group II and three from group III did not respond to the invitation. Data were therefore available for 78 (92%) of the still living individuals. Seventy-four individuals participated in the echocardiographic examination at follow-up in 2004–2006, and echocardiographic data were available from an earlier examination in one additional participant.

The participants answered questions about training status (similar to the questions answered in 1976 and 1981) and medical status. The questionnaires contained questions about physical activity, training and competing status between 1981 and follow-up in 2004–2006 and detailed questions about health status and heart disease, including self-reporting of the approximate date for the first diagnosis of AF.

The examination programme applied during the studies in 1976 and 1981 consisted of a physical examination, pulmonary function evaluation, electrocardiographic (ECG) recording during rest and exercise and a maximal cycle ergometer exercise test [19,20]. Maximal oxygen uptake (VO_{2max}) was predicted according to Astrand and Rhyming [21]. At follow-up in 2004–2006, the maximal exercise

Fig. 1



Flow chart for participating and missing cross-country skiers from baseline to follow-up. [a]The examination programme in 1976, 1981 and 2004–2006: resting and exercise electrocardiograph, maximal oxygen uptake, vitalographic assessment. Questionnaire: family history, health status, training and competing patterns. [b]Including echocardiography in 2004–2006. Eight participants from age group III did not perform the exercise test with exercise ECG, but did do resting ECG and echocardiography. One from group II did not do any examinations, but his record from a hospital with recent echocardiography and ECG was available. [c]Two in age group II had moved abroad in 1981, but participated in 2004–2006. Two in age group III refused to participate because of no cardiac diseases in 1981 and they were included in 'dead at follow-up in 2004–2006'. [d]Included one patient dead before 1981.

test was performed on a treadmill [22] by one investigator (J.G.) according to the guidelines of the ESC [23]. In group III, only resting ECG was taken. A flowchart for participating and missing individuals is shown in Fig. 1.

Complete two-dimensional M-mode and Doppler recordings at rest were obtained with a VingMed Vivid 7 (Vingmed Sound, Horten, Norway) echocardiograph. One investigator (I.G.) performed all of the echocardiograms using standard methods of measurements according to the recommendations of the American Society of Echocardiography [9,24].

We used data from the records from 1976 and 1981 when looking for possible predictors. ECGs were found in data from 1976 and 1981, read blindly, and PQ times were measured from the resting ECGs and noticed on the ECGs. Resting heart rates (HRs) were measured after 5 min in 1976 [19] and 10 min in 1981 [20] in the recumbent position. ECG criteria of LVH were analysed according to the Scandinavian modification of the Minnesota Code for ECG classification [25].

In this study, we have used the term LAF for all participants with AF without known structural heart disease at first diagnosis of AF, even if four participants were older than 60 years when diagnosed [26].

Data analysis was performed with the Statistical Package for the Social Sciences version 14 (SPSS 14, 2005; SPSS Inc., Chicago, Illinois, USA). Data from 1976 and 1981 were originally in paper version, and were transferred to the SPSS. The data were tested for normal distribution using quintile–quintile (QQ) plots. Differences between mean values were assessed with the unpaired Student's *t*-test and differences of proportions were assessed by the χ^2 test. A two-tailed P value of ≤ 0.05 was considered significant. Results are expressed as mean ± SD, if not otherwise described. Correlations or linear and multiple regression analysis were used to assess the impact of different parameters on AF or to assess correlations between other variables.

Results

The overall prevalence of AF occurring at any point of time during the entire follow-up was 16.7%, whereas the prevalence of LAF was 12.8%. The prevalence and age of appearance of AF in three different age groups and among all 78 participants is shown in Table 1. Table 2 shows that skiers number 3 and 13, with known coronary heart disease, developed AF at the age of 87 and 79 years, respectively. Skier number 1 with known AF from the age of 65 years was diagnosed with a persistent ductus arteriosus (PDA) at 73 years old, which could be the cause of AF. The remaining 10 participants without structural heart disease at the time of diagnosis developed AF at an average age of 57.9 ± 10.1 years. Table 2 also shows that skier number 6 had his first known appearance of paroxysmal LAF at the age of 46 years. Nine years later, he was diagnosed with sick sinus syndrome and was treated with an implanted pacemaker, and another 4 years later, he had a successful catheter ablation procedure. Skier number 10 was 64 years old at the first appearance of paroxysmal AF. Later, he was diagnosed with aortic stenosis (operated in 1995) and congestive heart failure. Skier number 7 had a transient ischaemic attack 1 year before the occurrence of AF. Previously undiagnosed AF was documented in skiers number 4 and 11. None of the participants with AF had hypertension.

Table 1 Prevalence of AF occurring at any point of time during the entire 28–30 years of follow-up among long-term endurance cross-country skiers

Age group; *n*	Age, mean ± SD (range) (years)	Number of participants with AF (%)	Age at which AF was detected, mean ± SD (range)[a]
I; 33	58.9 ± 2.2 (54–62)	6 (18.2)	52.7 ± 9.1 (38–62)
II; 37	74.8 ± 2.4 (72–80)	5 (13.5)	67.0 ± 8.5 (58–79)
III; 8	88.5 ± 1.7 (87–92)	2 (25.0)	75.5 ± 16.3 (64–87)
All; 78	69.5 ± 10.2 (54–92)	13 (16.7)	61.7 ± 12.8 (38–87)

AF, atrial fibrillation. [a]First diagnosis of AF.

Table 3 illustrates the echocardiographic parameters in patients with and without AF. Left atrial diameter and left atrial area were larger in the AF group than in the sinus rhythm group. Left ventricular ejection fraction was within normal range among all participants independent of rhythm; the significantly lower values among those with AF might be because of less precise measurement with an irregular rhythm.

Table 4 shows that the 10 participants with LAF had significantly lower resting HRs in 1981 and longer PQ times both in 1976 and 1981 compared with participants with sinus rhythm. No differences were identified with regard to blood pressure from 1976 and 1981 (data not shown) or for body mass, height, age, alcohol use or blood tests for hyperthyroidism at follow-up in 2004–2006. Table 4 also shows that there were no differences between groups in life-long self-reported hard training time in hours or hard training in years.

Significant correlation was found between long PQ time from 1976 and 1981 and AF ($r = 0.38$, $P = 0.001$ and $r = 0.27$, $P = 0.02$, respectively), and between low HR at rest from 1981 and AF ($r = 0.29$, $P = 0.012$). A significant correlation was found between HR and PQ time both in 1976 and 1981 ($r = -0.28$, $P = 0.013$ and $r = -0.23$, $P = 0.046$, respectively).

Age-adjusted VO_{2max} in 1976 or 1981 was not significantly correlated to LAF (data not shown). For left atrial

Table 2 Demographic, some clinical characteristics, LAD systolic and LAA systolic among long-term endurance cross-country skiers with AF

Skier	Age group/ age in years	Age at AF diagnosis (years)	Rhythm at follow-up	Concomitant disease-year	Medication	LAD systolic (mm)	LAA systolic (cm^2)
1	II/73	65	Chronic AF	PDA-2007	None	66	55
2	II/72	58	Chronic AF	None	Warf	45	41
3	III/87	87	Chronic AF	CHD-1997	Warf	44	22
4	II/72	72	Chronic AF	None	None	54	34
5	II/72	61	Parox AF	None	ASA + Flec	57	37
6	I/61	46	Pacemaker	Sick sinus-1999	None	47	23
7	I/62	60	Parox AF	TIA-2001	Warf + Flec	37	
8	I/57	55	Parox AF	None	Flec	47	30
9	I/61	38	Sinus rhythm	None	None	50	26
10	III/88	64	Chronic AF	CHF, AS-1995	Several	51	41
11	I/62	62	Parox AF	None	None	45	26
12	I/58	55	Sinus rhythm	None	None	49	33
13	II/80	79	Chronic AF	CHD	Several		

AF, atrial fibrillation; AS, aortic stenosis; ASA, acetylsalicylic acid; CHD, coronary heart disease; CHF, congestive heart failure; Flec, flecainid; LAA, left atrial area; LAD, left atrial diameter; Parox, paroxysmal; PDA, persistent ductus arteriosus; Sick sinus, Sick sinus syndrome; TIA, transient ischaemic attack; Warf, warfarin.

Table 3 Echocardiographic findings at follow-up in 2004–2006 among 33 cross-country skiers in age group I and 72 in all three age groups with and without LAF (excluding participants 1, 3, 10 and 13 in Table 2 with concomitant heart disease)

	Group I			All		
	Sinus ($n=27$)	LAF ($n=6$)	*P* value	Sinus ($n=63$)	LAF ($n=9$)	*P* value
LVD diastolic (mm)	55 ± 5	54 ± 3	NS	54 ± 4	53 ± 3	NS
IVS diastolic (mm)	10 ± 1	10 ± 1	NS	10 ± 1	10 ± 2	NS
LVPW diastolic (mm)	10 ± 1	10 ± 2	NS	10 ± 1	10 ± 1	NS
LVEF (%)	60 ± 6	53 ± 7	NS	58 ± 6	53 ± 6[a]	0.016
LAD systolic (mm)	42 ± 5	46 ± 6	0.12	43 ± 5	48 ± 6	0.013
LAA systolic (cm^2)	24.9 ± 3.6	27.6 ± 3.9	0.14	24.8 ± 3.9	31.3 ± 6.1[a]	< 0.001

Data are expressed as mean ± SD, unless otherwise specified. IVS, interventricular septum; LAA, left atrial area; LAD, left atrial diameter; LAF, lone atrial fibrillation; LVD, left ventricular diameter; LVEF, left ventricular ejection fraction; LVPW, left ventricular posterior wall; NS, not significant. [a]Data of eight participants.

diameter and left atrial area at follow-up, correlations with AF were found ($r = 0.41$ and 0.53, respectively; $P < 0.001$ for both). Multivariate regression analysis including both PQ time and HR at rest in 1976 and 1981, respectively, showed significant correlation between PQ time and LAF only (1976: PQ time: $P = 0.004$, HR at rest: $P = 0.6$ and 1981: PQ time: $P = 0.026$, HR at rest: $P = 0.058$).

In 1981, 55 and 20 participants presented with and without ECG criteria of LVH, respectively. The three skiers with AF and structural heart disease were excluded form this analysis. In the follow-up study in 2004–2006, nine of these 55 skiers (16.4%) had developed LAF versus one of 20 (5%) without LAF. However, this difference was not statistically significant (P=0.16).

Discussion

The currently reported prevalence of LAF of approximately 13% among all 78 skiers is the highest prevalence yet described in long-term endurance sport practitioners. The study has, in addition, found bradycardia and long PQ time as predictors for the occurrence of LAF. Finally, it was found that atrial enlargement, as cardiac adaptation to training, could be of importance in the development of LAF among athletes.

The first reports of a possible higher frequency of episodes of LAF in endurance athletes appeared in the late 1980s and 1990s [1,27,28]. In three different case–control studies, there was a significantly higher prevalence among the endurance athletes (5.3, 4.9 and 10%, respectively) compared with the controls [3,5,29]. Older age and longer follow-up time may explain the higher prevalence of 10% observed in the study by Baldesberger *et al.* [29] and 13% observed in our study. Mont *et al.* [14] suggest in their recently published review that the incidence of AF and flutter further increases with aging in athletes, which is supported by our data with a mean age of approximately 58 years at the time of diagnosis of LAF. However, we had a considerable dropout of 44 (mostly because of deaths in age group III) of the 122 cross-country skiers during the follow-up. The prevalence in each subgroup in our study must therefore be interpreted with caution because of the small sample sizes. Even if the prevalence of AF among all (16.7%) at a mean age of 70 years is not far from that described by Tveit *et al.* [6] in a 75-year-old male Norwegian population (15%), the prevalence of LAF (13%) is certainly higher. In the study by Tveit *et al.* [6], almost all had a structural heart disease (including hypertension) as a possible cause of their AF. Another factor is that the diagnosis of AF in our study was made mostly by history, which could result in the underestimation of the true prevalence, and particularly so for paroxysmal AF, because of possible asymptomatic AF and nocturnal vagal-mediated AF at night [11,14].

Low HR and long PQ time (interval) were associated with later appearance of LAF in our study. Slow HR at rest (bradycardia), large heart volumes and eccentric

Table 4 Possible predictors for LAF in 1976, 1981 and at follow-up in 2004–2006 in individuals with and without LAF in age group I and among all

	Group I			All		
Rhythm	Sinus ($n=27$)	LAF ($n=6$)	*P* value (95% CI)[a]	Sinus ($n=65$)	LAF ($n=10$)	*P* value (95% CI)[a]
HR rest, 1976	53.1 ± 9.3	44.0 ± 5.0	0.029 (1.0–17.1)	52.2 ± 8.6	48.3 ± 7.4	NS
HR rest, 1981	49.4 ± 8.0	41.0 ± 1.7	0.017 (1.6–15.2)	49.3 ± 7.5	42.9 ± 5.3	0.015 (1.3–11.6)
PQ time, 1976	0.17 ± 0.02	0.21 ± 0.05	0.001 (−6.5 to −1.9)	0.17 ± 0.02	0.20 ± 0.03	0.001 (−3.9 to −1.1)
PQ time, 1981	0.18 ± 0.03	0.22 ± 0.05	0.007 (−7.0 to −1.2)	0.18 ± 0.02	0.20 ± 0.04	0.020 (−3.9 to −0.4)
LLATH	13 625 ± 5051	15 266 ± 3619	NS	14 505 ± 5354	13 137 ± 4349	NS
Years HT	38.9 ± 10.0	42.2 ± 8.1	NS	43.2 ± 12.8	39.4 ± 10.9	NS
Height FU	179 ± 6	177 ± 3	NS	177 ± 7	179 ± 4	NS
Body mass index FU	24.2 ± 3.0	24.2 ± 0.9	NS	24.3 ± 2.6	23.6 ± 1.3	NS
FT4 FU	11.9 ± 1.8	10.4 ± 1.9	NS	11.5 ± 2.1	10.8 ± 2.8	NS
TSH FU	2.3 ± 1.4	3.0 ± 1.2	NS	2.4 ± 1.6	2.7 ± 1.0	NS
Alc FU	7.9 ± 10.1	6.8 ± 6.7	NS	7.4 ± 8.3	6.2 ± 6.3	NS

Data are expressed as mean ± SD, unless otherwise specified. Alc, self-reported units of alcohol consumed each weak (1 U is equivalent to 12.8 g alcohol); CI, confidence interval; FT4, TSH: test for hyperthyroidism; FU, follow-up; Height, height in cm; HR rest, heart rate at rest; LAF, lone atrial fibrillation; LLATH, long-life accumulated training hours; NS, not significant; PQ time, PQ interval; Years HT, years with hard training. [a]95% CI of the difference between groups.

hypertrophy are common findings in 'athlete's heart' among endurance athletes [30,31]. Even if not significantly different in our study with relatively few athletes, we found about three times the risk among those with ECG criteria of LVH compared with those without these criteria. Five more years with hard training from 1976 to 1981 [20] seem to have resulted in more participants with a possible 'athlete's heart' and increased risk for LAF. However, the results must be evaluated with caution, as we found left ventricular dimensions within normal upper limits both in those with and without LAF at follow-up. Cross-country skiers are among the athletes with the most distinctly abnormal changes on ECG [32], and bradycardia in athletes is associated with prolonged atrioventricular conduction time (AV block degree I), which in turn is associated with LVH [31]. Some authors have suggested the relationship between bradycardia/increased vagal stimulation and triggering of AF in athletes [4,10,33]. Both increased sympathetic activity during physical activity and increased vagal tone at rest may predispose to AF development [12,34]. We do not know whether the participants in our study had an adrenergically or a vagally induced AF (or both). However, our study is the first to show that those with the longest PQ time are more vulnerable to the development of AF later in life.

Our findings of left atrial dimensions are in accordance with others, who found that left atrial size was associated with LAF in endurance-trained athletes [4,5,11]. However, this is in contrast to the findings by Pelliccia *et al.* [16], where younger age could explain the low prevalence of 0.3% of LAF. The measurements of atrial dimensions were obtained after the appearance of AF in our study as in the studies by Mont *et al.* [11] and Molina *et al.* [5]. Atrial enlargement therefore could be a consequence of, and not the cause of, AF. In this study, we did not find any correlation between years with AF and atrial enlargement (data not shown). Thus, our data do support the findings of Mont *et al.* [11] that atrial enlargement together with other factors may be of importance in the development of LAF in long-term endurance athletes [14]. However, in one recent study, successful pulmonary vein isolation with catheter ablation procedure has shown that the atrial remodelling may not play a decisive role in the maintenance of LAF in athletes [12,35], leaving this question still unanswered.

We did not find any correlation between years of practice of cross-country skiing or life-long accumulated hours of hard training and appearance of LAF. As in our study, Molina *et al.* [5] did not find any association between hours of lifetime sport practice and LAF, but also in that study the amount of accumulated hours of training was above the hours needed for the higher risk described by Mont *et al.* [11]. In our study, the participants with LAF had more than 36 years of sporting practice before the first self-reported or known appearance of LAF, which is in accordance with the study by Karjalainen *et al.* [3], but higher than in the studies by Hoogsteen *et al.* [29] and Mont *et al.* [11]. However, long-time sport practice in middle-aged individuals seems to be an important factor for the increased risk of LAF in athletes [4,14,17]. Despite the increased risk for AF among long-term endurance athletes, it is still not enough evidence to recommend a specific age to reduce training volume and/or intensity [14]. After the appearance of LAF, it is so far recommended to stop or reduce sports practice until rhythm control is attained [36]. However, a few athletes treated for their AF with radiofrequency catheter ablation could in one study go back to their former training and competition pattern [35].

A limitation of the study was that we did not have any control group. The study was uncontrolled with regard to training volume and intensity, but was based on self-reported training time in hours per week and number of years of unchanged training patterns. Many participants continued to train many hours per week despite reported reduced training volume, but we do not have data on high intensity training from 1976 and 1981 until follow-up. Some of the results could be biased, because of small numbers of participants in subgroups. Unfortunately, we did not have former echocardiographic data.

Conclusion

This study provides evidence that LAF is more common in long-term endurance-trained cross-country skiers than in men in the general population. Predictors from 1976 and 1981 for LAF were a long PQ time at upper normal limits and a low resting HR. Left atrial enlargement was associated with LAF at follow-up after 28–30 years. We still do not know why some athletes end up with LAF and others do not. Genetic factors predisposing to 'athlete's heart' with enlarged cardiac dimensions, increased vagal tone and prolonged atrioventricular conduction time might be of importance as risk factors. Hopefully, further research will unravel such predisposing factors.

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IV

Mortality and cardiovascular morbidity among long-term endurance male cross-country skiers followed for 28-30 years.

Running head: Cardiovascular disease among X-C skiers.

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Abstract

Background Longevity and reduced CVD mortality and morbidity compared to the general population are described among former elite athletes in a few studies only.
Aim To assess the outcomes of mortality and CVD morbidity after 30 years follow-up in long-term trained cross-country skiers and to examine possible risk predictors for later appearance of CVD and CHD (coronary heart disease).
Methods The study was based on 122 long-endurance cross-country skiers participating in studies in 1976 and 1981. A total of 78 out of 85 skiers completed the 28-30 year follow-up, while 37 were dead. Causes of death through 2006 were ascertained using the National Death Register. Morbidity data were available in 115 subjects.
Results Total deaths were 31 % compared to 40 % in the general male population (p=0.04). Exercise-ECG ST-depression in 1981 was associated with later appearance of CHD (HR 2.90; p=0.033). BMI and average systolic blood pressure (SBP) from 1976/1981 were predictors of later appearance of CVD (HR 1.23; p=0.034 and HR 1.03; p=0.048, respectively). Among the still living (age 67.3 ± 8.3 yrs: range 51-92 yrs) low prevalence of CHD (14.1 %), diabetes type II (2.6 %), hypertension (11.5 %) and BMI > 30 (1.3 %), and favourable risk factors with 5.1 % smokers, high HDL: 1.8 ± 0.4 mmol/l, low total cholesterol/HDL ratio: 3.4 ± 1.0, and low SBP: 122 ± 13, were found.
Conclusion Long-term aerobic exercise appears to be associated with reduced all-cause mortality and morbidity and favourable CVD risk factors.

Keywords: longevity, long-endurance training, long-term follow-up, cardiovascular, risk factors

Introduction

Regular physical activity and high levels of aerobic capacity are associated with reduced risk of cardiovascular disease (CVD) and cardiovascular and all cause mortality [1,2,3,4]. The classical evaluation of cardiovascular risk estimation is based on four CVD risk factors: age, serum cholesterol, resting systolic blood pressure and smoking status [5,6], while the most recent version of the European Guidelines on CVD prevention also includes diabetes, the metabolic syndrome, obesity and physical inactivity as risk factors for CVD and reduced life expectancy [7]. Short-term risk of sudden coronary events is increased during vigorous exercise, and coronary heart disease (CHD) is the main underlying cause of sudden cardiac death among the ageing adult athlete [8,9]. Reduced mortality and longevity (because of lower CVD mortality) among former elite distance runners and cross-country skiers as compared to the general population are described in a few studies only [10].

In a 26 years CHD mortality and 22 years CHD morbidity study Bodegard et al. [11] found that electrocardiographic (ECG) ST-depression during and/ or after exercise testing increased the long-term risk of fatal or non-fatal CHD in healthy middle-aged men. In a study population of 122 long-term endurance cross-country skiers in three different age groups no significance of a positive exercise test was found after five years follow-up [12]. The same groups of cross-country skiers were presently examined in a follow-up study after 28-30 years [13,14].

The aim of this follow-up study was to (i) report the outcomes of mortality and cardiovascular morbidity in this cohort of cross-country skiers after 28-30 years, (ii) examine if known risk factors were predictors for later appearance of cardiovascular disease or cardiac death and (iii) analyse if ST-depression in an exercise test 23-25 years earlier was predictive of CHD-mortality or morbidity and (iv) examine if a lifestyle with long-time endurance training had protective effects on known risk factors at follow-up among these former and/or current highly trained athletes.

Population and methods

In 1976 Lie & Erikssen [15] examined 122 healthy male Norwegian cross-country skiers in three preselected age groups, who for many years had been among the best quartile in different endurance cross-country competitions. All were recruited from the 58 km long Norwegian 'Birkebeiner' cross-country race. The material and criteria for entering the study are described in detail elsewhere [13,15]. In a five-year follow-up study 117 men participated [16]. All men still alive from the original population were asked to participate in this present follow-up study. The Norwegian Regional Ethical Committee approved the study protocol. Permission to contact the participants and look into their medical and death certificates were given from the Norwegian Data Inspectorate and the Norwegian Board of Health. All of the participants provided informed consent to the approved study protocol, and 78 subjects participated in the follow-up study in 2004 – 2006. Out of the original 122 subjects, 37 (30 %) had died during the period from 1976 to 2006, with 1/35 in age group I, 8/48 in group II and 28/39 in group III. Cause-specific mortality data up to 31 December 2006 were obtained from death certificates provided by Norwegian National Registry. All death certificates were coded according to the *International Classification of Diseases* (ICD). Deaths between 1969-1985 and 1986-1995 were coded according to the Norwegian versions of ICD-8 and ICD-9, respectively, while deaths from 1996-2006 were coded according to the English version of ICD-10. Mortality and morbidity data from 1976 until follow-up in 2004-2006 or until the date of death were available in 115 subjects, and data from the Norwegian population register proved that the six men who did not respond to the invitation still were alive at the end of

2006. Only one man was not found in the central Norwegian population register and was therefore missing in this follow-up study.

The studies in 1976 and 1981 included a medical history with particular information on indices of angina pectoris, smoking habits and CHD in first degree relatives [15,16]. The 78 still living subjects answered questions about life-long training and competition patterns and history, identical to the questions answered in the two earlier studies [15,16]. In addition they answered questions about life-style (including earlier and current smoking habits) and medical status including detailed questions about cardiovascular and other diseases as diabetes and cancer from 1981 until follow-up.

The blood tests in the two former studies included serum total cholesterol (TC), serum triglycerides (TG) and serum high density lipoproteins (HDL) (HDL only in the study in 1981). All samples were analyzed in the Central Laboratory of Oslo University Hospital, Ulleval [16]. At follow-up in 2004-2006 the blood samples included TC, TG, HDL, and serum low density lipoproteins (LDL: calculated according to Friedewald's formula) and glycated haemoglobin (HbA1C) analyzed at Akershus University Hospital, Eidsvoll for age group I and II and at Oslo University Hospital, Ulleval, Oslo for age group III. (The same tests and procedures were used at both laboratories).

The examination programme during the studies in 1976 and 1981 is described in detail elsewhere [15,16]. The resting and exercise ECGs were classified according to the Scandinavian Modification of the Minnesota Code, where the criteria for a pathological exercise ECG (4.1 changes) were ST-depression of $\geq$ 1.5 mm 0.08 sec. from the J-point in the precordial leads V2-V6, or $\geq$ 1.0 mm in leads I, II, III, aVL or aVF [17]. The examination programme and the maximal exercise test at follow-up are described in detail elsewhere [13,14].

Statistical Analysis

Continuous variables were tested for normal distribution using quintile-quintile (Q-Q) plots. Differences between mean values were assessed with the unpaired Student *t* test if normally distributed; otherwise the Kruskal-Wallis test was used. Results are expressed as mean ± SD. Categorical variables were assessed by Fisher's exact test or chi-square test as appropriate. Age-adjusted correlations or linear regression analyses were used to assess associations between different parameters**.** A two-tailed p value < 0.05 was considered significant. Differences between observed and expected proportions were tested using the binomial probability test.

Univariate analyses of survival from all-cause mortality and survival free of CVD and/or CHD were performed using Kaplan-Meier product limit estimator and log-rank tests. Survival adjusting for baseline risk factors was evaluated in a multivariate Cox proportional hazard model. The Cox model was built by a forward selection procedure The assumption of proportional hazards was checked using log-log survival plots and tests based on Schoenfeld residuals. Continuous covariates were evaluated for linearity in log hazard. Interaction terms were kept in the model if they were statistically significant and biological interesting. The survival analyses were conducted by using STATA software version 11 (College Station, Texas, USA).

Results

Table 1 shows numbers and causes of deaths in the three different age groups. Average age of deaths among all was 75 ± 9 yrs (range 51 - 90 yrs), with 51 yrs in age group I (n = 1/34), 68

yrs (range 58 – 75 yrs) in age group II (n = 8/48) and 78 yrs (range 62 – 90 yrs) in age group III (n = 28/39). Approximate average age in the three original groups if all were alive at the end of 2006 would have been 76 yrs among all and 60 yrs, 77 yrs and 90 yrs for age groups I, II and III, respectively. Total deaths in our population was 37/121 (31 %) compared to 40 % at the same average age in the general Norwegian male population ($p = 0.04$). In age group I: 3 % were dead (one man only) compared to an expected age-matched death rate of 10 % ($p = 0.25$: typical statistical type II error), in age group II: 17 % of the men were dead compared to an expected age-matched death rate of 40 % ($p = 0.001$) and in age group III: 72 % were dead compared to the expected age-matched death rate of 90 % ($p = 0.001$). Fig. 1 shows Kaplan-Meier estimates of survival in the different age groups. Among those dead at an age younger than 80 yrs 67 % had died of CVD compared to 40 – 50 % (depending on the death year: Norwegian National Registry) in the general male Norwegian population. Only one or two subjects seem to have suffered an acute cardiac death during or short after training, but the data about sudden cardiac death on the death certificates are uncertain. No one died suddenly during competitions.

Table 2 shows the prevalence of CVD, CHD and cancer among all 115 and among the 78 subjects still alive during the follow-up period of 30 years. As many as 42.6 % among all and 24.4 % among those still alive had experienced CVD, while the prevalence of cancer was 11.3 % and 5.1 % among all and among those still alive, respectively. Only two men (both in age group I) had diabetes mellitus type II (DM II) and one of them also had CHD at follow-up. They were the only two men who had stopped training in age group I, and their BMI (kg/cm2) had changed from 27.3 to 30.1 and 25.6 to 29.1, respectively, from 1976 to follow-up after ≈ 29 years.

Table 3 shows different CVD risk factors (average data from 1976 and 1981) among all and from follow-up in 2004-2006 among the men still alive. Among the still living subjects at follow-up SBP was increased with increasing age ($r = 0.42$, $p < 0.001$), while TG was decreased with increasing age ($r = 0.29$, $p = 0.016$). HbA1C at follow-up was only elevated (> 6.0 mmol/l) in the two subjects with DM II (5.4 ± 0.7 mmol/l among all) (data not shown). There was no difference between age groups. At follow-up 13 men were on medical treatment with statins and 17 on antihypertensive medication. There were no longitudinal changes in TC (5.9 ± 0.9 mmol/l vs. 6.0 ± 1.3 mmol/l; $p = 0.31$) among those without statins (n = 59: 13 on statins, 6 missing values), but a raise in TG from 1.21 ± 0.34 mmol/l to 1.45 ± 0.81 mmol/l ($p = 0.026$). HDL (n = 53) was significantly increased from 1981 to follow-up from 1.4 ± 0.3 mmol/l to 1.9 ± 0.4 mmol/l ($p<0.001$). TC/HDL-ratio improved significantly among 53 subjects (with HDL-values both in 1981 and at follow-up and without statins) from 4.1 ± 0.9 to 3.4 ± 1.0 ($p<0.001$; CI of the difference: 0.4 – 1.0). However, these results must be interpreted with caution because of different laboratory methods between baseline (average values from1976/1981) and follow-up (2004-2006). There was a significant longitudinal decrease in blood pressure (average blood pressure from baseline to follow-up among those without anithypertensive medication (n = 57) with SBP of 132 ± 9 mmHg vs. 122 ± 12 mmHg ($p<0.001$) and DBP of 89 ± 6 mmHg vs. 73 ± 8 mmHg ($p<0.001$), respectively (data not shown).

All together 33 % were former smokers (table 3), while only 7 % were still smoking in 1976 [15]. There was a significant difference in numbers of former smokers between age groups I and II ($p = 0.001$) and age groups I and III ($p = 0.002$), respectively, while no difference between age groups II and III was found. Twenty-three former smokers still alive stopped smoking 40 ± 17 years ago (range 3 – 71 years). Only two had stopped smoking less than 10

years ago (3 and 8 years, respectively). The four subjects still smoking smoked from 0.2 to 4 cigarettes per day. Among the dead we do know that there were only 2 current smokers in 1976, while 11 had been a former smoker (data not shown) [15]. There was no age-adjusted correlation between 'former smoker' and fatal or non-fatal appearance of CVD (data not shown). There was reported a history of CHD in first degree relatives in 32 men [15]. No correlation was found between family history of CHD and later appearance of CHD or CVD (data not shown). Neither was there found any correlation between age-adjusted average VO2max from 1976/1981 and later appearance of CVD (data not shown).

Cox regression analysis showed that age as a continuous variable was not linear in ln hazard and was thus entered as age groups coded as dummy variables with reference coding with the youngest age group as reference group. In the multivariate analyses ST-depression in an exercise test in 1981 was associated with later appearance of CHD (table 4 and fig. 2), but not with CVD. BMI and average systolic blood pressure from 1976 and 1981 were predictors for later appearance of CVD (table 4 and fig. 3a and 3b). Hazard ratio for 5 mmHg increase in SBP was 1.15 (CI 1.00 – 1.32), while hazard ratio for 5 units increase in BMI was 2.87 (CI 1.09 – 7.59) for CVD and 3.00 (CI 0.90 – 9.98) for CHD.

Discussion

The effects of long-term endurance training on all cause mortality and cardiovascular mortality and morbidity have only been studied in a few studies, and the need for further studies are warranted (10,18). In the present study mortality and cardiovascular morbidity data after almost 30 years follow-up is presented evaluating predictions of known risk factors. In addition the predictive value of ECG ST-depression in an exercise test 25 years earlier is described. The main findings were that (i) long-term endurance male cross-country skiers live longer than males in the general Norwegian population; (ii) CVD was the main cause of death during the 30-yrs study period; (iii) ST-depression in an exercise test 23-25 yrs earlier was a predictor for later appearance of CHD mortality and morbidity, while BMI and SBP were predictors of CVD; and (iv) long-term endurance training had positive effects on several known risk factors for CVD as HDL-cholesterol, TC/HDL-ratio, blood pressure and evolving DM II.

Exercise capacity and physical fitness are inversely related to mortality risk in healthy individuals [18,19,20]. This has also been found among the very old physical active people [21]. The cross-country skiers in the present study have an increased life expectancy compared to the general male population [22]. They had a high exercise capacity both in 1976 and 1981 with approximately 150 % of predicted age-related values [15,16]. The exercise-tested 68 subjects still had a very high exercise capacity at follow-up [13]. Among the dead the average age the last time they competed was 57.4 ± 9.8 yrs in age group II and 67.7 ± 6.5 in age group III, while the average age between the last competition and the death year was 10.2 ± 9.1 (data not shown), indicating that they had a life-long high exercise capacity, even if we do not know their exact physical fitness status from the last time they competed until the death date. The findings about longevity among former highly trained cross-country skiers in the present study support the findings by Karvonen et al. [23], Sarna et al. [24] and Chakravarty et al. [25] of increased life expectancy among Finnish cross-country skiers, Finnish world class male endurance athletes (cross-country skiing and long-distance running) and British runners, respectively.

Not only exercise capacity and regular exercise training, but also favourable influence on known risk factors (less smokers, improved lipid profiles and lower blood pressures) may lead

to increased life expectancy among the cross-country skiers in this study. Only 5.1 % of the subjects in the present cohort were still smokers at follow-up, compared to more than 20 % among men in the general Norwegian population [26]. In addition only 3 men dead at follow-up were still smoking in 1976, while 11 had been a former smoker. Smoking habits changed considerably among all subjects from the time before the first study in 1976 (33 % had been a former smoker) until 1976, when only 6.6 % were still smokers. This tendency of reduced numbers of smokers is also described in a study among men from the general Norwegian population [27]. Very few smokers compared to the general male Norwegian population are supposed to contribute to the reduced all-cause mortality among the men in this cohort. The low prevalence and deaths of cancer may also be due to few smokers and regular physical activity [28].

Among healthy male cross-country skiers, ST-depression in an exercise test predicted CHD mortality and morbidity during 25 yrs of follow-up, independently of age, systolic blood pressure, serum cholesterol, family history of CHD, physical fitness measured as VO2max and BMI. Only 'age group' was predictive for all-cause mortality, while systolic blood pressure and BMI predicted CVD mortality and morbidity. The prognostic value of exercise-induced ST-depression as a predictor of long-term CHD/CVD mortality and morbidity has previously been described in healthy middle-aged men [11,29]. Our study is the first to show that exercise-induced ST-depression was a predictor of later CHD also in a group of highly trained male cross-country skiers. None of the traditional risk factors (blood pressure, cholesterol, smoking or family history of CHD) adjusted for age were predictors of later CHD.

TC and resting SBP from 1976/81 among all were 6.2 ± 0.9 mmol/l and 138 ± 13 mmHg, respectively (table 3), while TC/HDL-ratio among all were 3.4 ± 0.9 (data not shown), indicating that most of the subjects had acceptable protective values of these variables. Together with a very low number of smokers and persons with obesity they were supposed to have a low CHD mortality risk ratio [5]. Still, as many as 67 % of those dead before the age of 80 yrs had died of CVD (mostly CHD) compared to about 50 % found in a study by Stavem et al. [27] in men from a general Norwegian population and in studies in the European countries [30]. This indicate that an active lifestyle with long-term endurance training is protective at younger ages, but not so at older ages, where CVD is the main cause of deaths. Relative few subjects in the present study and low prevalence of cancer and other diseases may explain the high frequency of CVD deaths compared to other studies. The long-term cross-county skiers in our study live long and usually die of CVD at higher ages.

Thirteen subjects used statins and 17 antihypertensive medications in age groups I and II among the subjects still alive at follow-up. There was a significant difference in TC between those who used statins compared to those without, with 6.0 ± 1.1 mmol/l (range 3.6 – 8.3) vs. 4.9 ± 0.8 mmol/l (range 3.5 – 6.2) ($p < 0.001$). No difference in SBP was found between those on antihypertensive medication or not (121 ± 12 mmHg vs. 123 mmHg ± 13). The findings among those without medication were comparable to the results in the study by Schroeder et al. [31], who found values for total cholesterol of 5.6 mmol/l and SBP of 131 mmHg among older runners aged 60 yrs. The latter results were lower than reported in the literature for sedentary adults at the same age. We found no longitudinal change in TC. TC at follow-up among all in age group I and II were approximately as reported among 60 yrs and 75 yrs old men in the general Norwegian population (5.8 mmol/l vs. 5.9 mmol/l and 5.7 mmol/l vs. 5.6 mmol/l, respectively) [32]. Protective high values of HDL-cholesterol at follow-up in our study were approximately the same as in the study by Schroeder et al. (1.8 mmol/l vs.1.7

mmol/l). We found a significant increase in HDL and reduced TC/HDL-ratio during 25 years of ageing. Physical activity is one of few known factors that increase HDL [33].

Kujala et al. [34] found a prevalence of 9.1 % for ischemic heart disease, 1.7 % for diabetes, 20.0 % for hypertension and 2.3 % for BMI > 30 among 330 men aged 61.6 yrs (range 43-90 yrs) engaged in endurance sports (long-distance running and cross-country skiing). Age-adjusted odd-ratio values for all four parameters were significantly different from values of 777 sedentary referents with a mean age of 55.0 yrs (range 38-86 yrs), who had prevalence of 19.4 %, 6.7 %, 28.6 % and 12.3 % for ischemic heart disease, diabetes, hypertension and BMI > 30, respectively. In our older cross-country skiers with a mean age of 67.3 ± 8.3 yrs (range 51-92 yrs) the corresponding prevalence were 14.1 %, 2.6 %, 11.5 % and 1.3 %, showing low values especially for hypertension, but also for the three other conditions compared to the 12 year younger referents in the study by Kujala et al. [34]. The prevalence of CVD, raised blood pressure and diabetes type II increase with age [35], indicating relatively lower prevalence in our population.

A major limitation of the present study is that we did not have any sedentary group for comparison from 1976 until follow-up after 30 years. In this longitudinal cohort study we have based the comparisons on comparable studies or statistics from the general Norwegian population (Norwegian National Registry). Epidemiological studies are in general in need of many participants for making meaningful statistical conclusions. One limitation to our study is the relatively small study group. However, we succeeded to include more than 90 % of the still living subjects, and had a complete registration of death causes. We studied three different age groups of long-time highly trained endurance cross-country skiers being among the top 25 % in the various regional contests at the start of the first study in 1976, but no one was top elite athletes. The results may therefore not be representative for top elite cross-country skiers or to other endurance athletes, though our findings support the findings in the few studies available about longevity among former top level endurance cross-country skiers and runners. However, the results may be representative for a larger group of highly trained men. Initially the inclusion criteria were only based on the results from ski contests, excluding possible biases as working status or social classes, which are known to be confounding factors (36). Most of the participants in the present study belonged to the three highest (out of five) social classes (37). It is known that persons in the higher social classes have better life expectancy than those in the lower (36). Finally, different laboratory methods of assessing blood parameters from baseline to follow-up were used, which could have lead to some variability; a common problem in longitudinal studies. Unknown confounding factors not included in our Cox models could have influenced the results, such as dietary habits, psycho-social factors and genetic endowments.

Conclusion

This study support the findings in the few longitudinal studies available that long-term trained male endurance athletes live longer than males in the general population. CVD was the main cause of death contributing to 57 % of total mortality. Increasing age was the only predictor of all-cause mortality. Electrocardiographic ST-depression in an exercise test was a predictor for CHD morbidity and mortality, while higher systolic blood pressure and higher BMI was predictors for later CVD morbidity and mortality. The cross-country skiers had favourable preventive risk factors for CVD with low systolic blood pressure and favourable TC/HDL-ratio. In addition they had low body mass index and there were almost only non-smokers. They had low prevalence of cancer, diabetes, hypertension and obesity. Long-term aerobic exercise appears to be associated with reduced all-cause mortality and morbidity.

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Tables

Table 1. Numbers (%) of cardiovascular, other causes and all-cause mortality among three different age groups of 121 former long-term endurance cross-country skiers.

	CHD	Other CVD	Cancer	Other diseases	Accidents	All-cause
Group I n = 34	1 (2.9)	0	0	0	0	1 (2.9)
Group II n = 48	4 (8.3)	1 (2.1)	0	2 (4.2)	1 (2.1)	8 (16.7)
Group III n = 39	8 (20.5)	7 (17.9)	9 (23.1)	2 (5.1)	2 (5.1)	28 (71.8)
All n = 121	13 (10.7)	8 (6.6)	9 (7.4)	4 (3.3)	3 (2.5)	37 (30.6)

CHD: coronary heart disease (myocardial infarction); CVD: cardiovascular disease; Accidents (incl. 1 suicide).

Table 2. Prevalence of CVD (CHD) and cancer in numbers (%) among all and among those < 80 yrs (groups I and II) in groups of both dead and alive (DA) and in those still alive (A) only.

	All DA n = 115	< 80 yrs DA n = 79	All A n = 78	< 80 yrs A n = 70
CVD	49 (42.6)	33 (41.8)	19 (24.4)	18 (25.7)
(CHD)*	24*(20.9)	15*(19.0)	11*(14.1)	10*(14.3)
Cancer	13 (11.3)	3 (3.8)	4 (5.1)	3 (4.3)

CVD: cardiovascular disease (included CHD and stroke; CHD: coronary heart disease. * included in CVD.

Table 3. Different cardiovascular risk factors from baseline (average data from 1976 and 1981) and from follow-up in 2004-2006 among all and among the three different age groups of long-term endurance cross-country skiers.

	Age group I (n)	Age group II (n)	Age group III (n)	All (n)
Age in yrs FU	58.9 ± 2.2	74.8 ± 2.4	88.5 ± 1.7	69.6 ± 10.2
(range)	(54-62)	(72-80)	(87-92)	(54-92)
BMI 76 in kg/m2	22.4 ± 1.5 (35)	22.8 ± 1.4 (48)	22.8 ± 1.6 (39)	22.6 ± 1.5 (122)
BMI FU in kg/m2	24.2 ± 2.8 (32)	24.0 ± 2.2 (36)	24.6 ± 3.2 (6)	24.1 ± 2.6 (74)
Total cholesterol[a]	5.6 ± 0.9 (34)	6.2 ± 0.8 (48)	6.6 ± 0.8 (39)	6.2 ± 0.9 (121)
Total cholesterol[a] FU	5.8 ± 1.1 (33)	5.7 ± 1.1 (33)	6.2 ± 0.9 (4)	5.8 ± 1.1 (70)
HDL cholesterol[a] 81	1.3 ± 0.3 (29)	1.5 ± 0.3 (47)	1.5 ± 0.3 (35)	1.4 ± 0.3 (111)
HDL cholesterol[a] FU	1.8 ± 0.4 (32)	1.8 ± 0.4 (33)	2.0 ± 0.4 (5)	1.8 ± 0.4 (70)
LDL cholesterol[a] FU	3.3 ± 0.9 (31)	3.4 ± 0.8 (33)	3.6 ± 0.6 (5)	3.4 ± 0.9 (69)
Triglycerides[a]	1.2 ± 0.4 (34)	1.2 ± 0.3 (48)	1.6 ± 0.7 (39)	1.3 ± 0.5 (121)
Triglycerides[a] FU	1.7 ± 0.9 (32)	1.2 ± 0.5 (33)	1.4 ± 0.9 (5)	1.4 ± 0.8 (70)
Systolic BP[b]	130 ± 9 (34)	135 ± 11 (48)	149 ± 12 (39)	138 ± 13 (121)
Systolic BP[b] FU	116 ± 10 (32)	126 ± 12 (36)	132 ± 21 (6)	122 ± 13 (74)
Famhist of CHD n (%)	7 (20.6)	12 (27.1)	13 (33.3)	32 (27.3)
Current smoker n	1	3	0	4
Former smoker n (%)	3 (8.8)	21 (43.8)	15 (40.5)	39 (32.8)
Diabetes FU n	2	0	0	2
Stopped training FU n	2	6	8	16

FU: follow-up in 2004-2006; BMI: body mass index; BP: blood pressure; Famhist: family history; CHD: coronary heart disease. [a] mmol/l; [b] mmHg.

Table 4. Hazard ratios (HR) for predictors for later appearance of fatal or non-fatal CHD/CVD diagnosis according to Cox analysis among 115 healthy cross-country skiers followed up for 25- 30 years.

	CHD	(n = 24)		CVD	(n = 49)	
	HR	95 % CI	p value	HR	95 % CI	p value
ST depression in 1981 (n = 23)	2.90	1.09 – 7.72	0.033			
Age group II (n = 48)	3.96	1.11 – 14.14	0.033	2.30	0.96 – 5.53	0.063
Age group III (n = 39)	3.46	0.87 – 13.82	0.078	2.04	0.73 – 5.76	0.176
Systolic blood pressure*				1.03	1.00 – 1.06	0.048
BMI§	1.25	0.98 – 1.58	0.073	1.23	1.01 – 1.50	0.034

*Mean values from 1976 and 1981; § BMI, body mass index. CI: confidence interval.

Figure legends:

Figure 1.

Kaplan-Meier estimates of survival in three different age groups (n=121) of long-term endurance cross-country skiers followed for 30 years. (For exact data confer text).

Figure 2.

Survival curves from the Cox model for individuals with or without electrocardiographic ST-segment depression in an exercise test 25-years earlier. The difference in survival free of fatal or non-fatal CHD between groups is significant (p = 0.033; confer table 4).

Figure 3a.

Survival curves from the Cox model for individuals with normal (120 mmHg), slightly elevated (140 mmHg) and elevated (160 mmHg) systolic blood pressure (mean values from 1976 and 1981). The difference in survival free of fatal or non-fatal CVD between groups is significant (p = 0.048; confer table 4).

Figure 3b.

Survival curves from the Cox model for individuals with three different values of body mass index (BMI in kg/cm2). The difference in survival free of fatal or non-fatal CVD between groups is significant (p = 0.034; confer table 4).

Figures:

Figure 1:

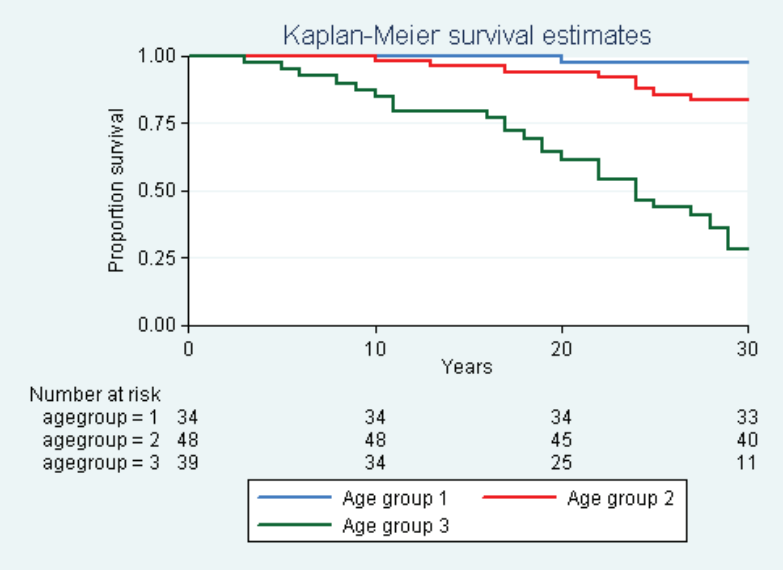

Figure 2:

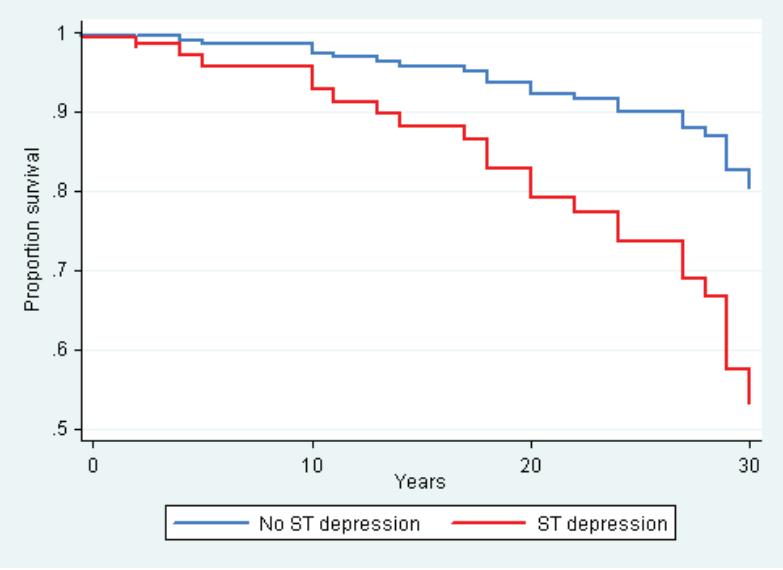

Figure 3a:

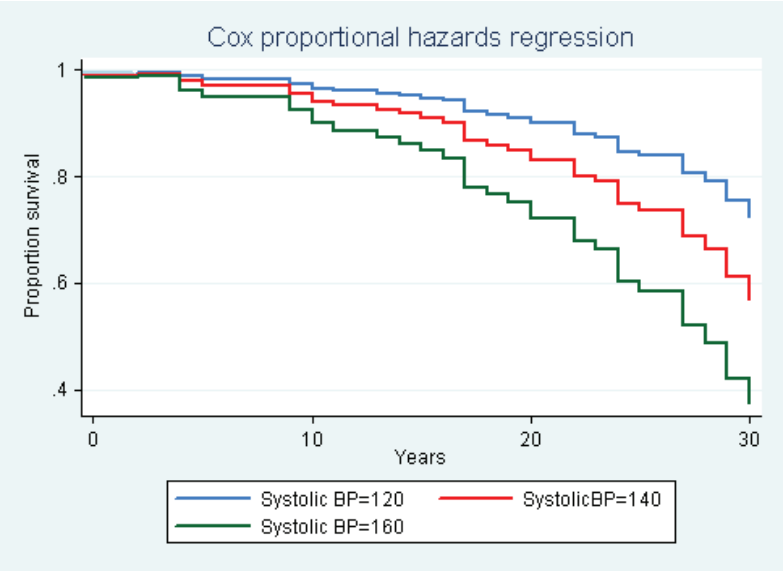

Figure 3 b: