Atrial fibrillation, physical activity and endurance training

Summary

Introduction. Clinical practice and the results of some studies may indicate that physical exercise in the form of endurance training may influence the development of atrial fibrillation (AF). The aim of this paper is to evaluate the scientific background for the hypothesis that there is a connection between physical activity and AF.

Material and method. This paper is a review article based on searches in PubMed on specific topics, limited to the period 1995 through March 2011. We found 17 original articles and three relatively recent reviews. Each was read by at least two of the authors and then discussed. Seven of the original articles were excluded for methodological reasons, and we therefore discuss the other ten.

Results. We found support for the hypothesis that systematic high intensity endurance training such as running can increase the risk of AF, whereas the studies provide no evidence that less intensive physical exercise such as walking increases the risk. Several of the studies have methodological weaknesses.

Interpretation. Important questions remain unanswered. There is a need for more studies that can shed light on the connection between training intensity, total volume of intensive endurance training, age-related changes and AF. Studies that include women are also needed.

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In long-distance running circles and among cardiologists there has long been an impression that the development of atrial fibrillation (AF) may be linked to long-term physical training. In this article we review published articles that may shed light on the question of whether physical activity of low or moderate intensity or in the form of systematic high intensity endurance training can increase the risk of atrial fibrillation.

Atrial fibrillation is characterised by irregular contractions of the atria with a frequency of 350–480 per minute (1). Only some of the impulses feed through the conduction system to the ventricles because the atrioventricular node functions as a filter, and QRS complexes will occur at irregular intervals on the ECG. Atrial fibrillation may occur as bouts or be permanent. As a rule, the peripheral pulse rate will be higher than normal both at rest and with exertion. Some people tend to experience bouts of fibrillation at night or after meals; with others, they accompany physical or mental strain. With most people, however, there are no clear patterns. The concept «lone atrial fibrillation», LAF, has been used since the 1950s in cases where there is no other known cardiac or metabolic disease.

Overall, the prevalence of atrial fibrillation in western countries is estimated to be 1–2 % of the population (1). Prevalence increases with age, from < 0.5 % at the age of 40–50 to 5–15 % at the age of 80. It is somewhat higher in men than in women, and has increased over the past few decades (1). It is estimated that some 65 000 Norwegians are affected by atrial fibrillation, and that 20 000–25 000 of them are under the age of 67 years (2). A Norwegian survey conducted in 2008 found a prevalence of 10 % among 75 year-olds in Asker and Bærum, near Oslo (3). Apart from age and gender, the established risk factors for atrial fibrillation are underlying cardiac disease, chronic pulmonary disease, metabolic disorders, hypertension, diabetes, overweight, sleep apnoea and chronic renal disease (1).

Factors regarded as important in the development of the disease are structural changes to the heart, particularly in the atrial musculature, changes in electrophysiological mechanisms and genetic disposition (1). Structural changes may involve fibrosis, inflammation, necrosis, hypertrophy and microvascular changes. When atrial fibrillation first does occur, the condition in itself will affect the myocardium, prompting an increased tendency to fibrillation. In the case of paroxysmal atrial fibrillation, the individual attack usually starts from focal points in or near the transition between the pulmonary veins and the left atrium; with persistent atrial fibrillation, the impulses are maintained because of general changes in the atria. In recent years, genetic research has contributed to identifying a series of poly-

Main message

- Relatively high intensity endurance training for many years probably increases the risk of atrial fibrillation, at least in men aged over 40.
- Less intense exercise almost certainly does not increase the risk of atrial fibrillation.
- Many studies of physical activity and atrial fibrillation have major methodological weaknesses.

Table 1 Physical activity and atrial fibrillation in cohort studies

Study (first author, year)	Proportion of men (%)	Measure of physical activity	Relative risk (RR) (95 % CI)
Aizer A, 2009 (10): Selected healthy doctors aged 40–84 (n = 16 921), followed for 12 years Atrial fibrillation self-reported by validated method	100	Questionnaire on amount of intensive exercise/week, type of activity and distance, if running	RR 1.2 (1.0–1.4) with daily intensive vs no training < 50 yrs: RR 1.7 (1.2–2.5) with daily intensive vs no training
Mozaffarian D, 2008 (11): Healthy elderly general population ≥ 65 (n = 5 446), followed for 12 years Atrial fibrillation identified by ECG, Holter monitor, journals and discharge diagnoses	42	Questionnaire on amount of exercise, intensity and distance walked	Graded *lower* risk of atrial fibrillation with light to moderately intensive exercise (walking) vs no exercise. Intensive exercise: as with the sedentary

morphisms associated with atrial fibrillation. Heredity is particularly important when the condition occurs at a young age (1).

The complications of atrial fibrillation are degraded quality of life and work capacity, higher death rates and increased risk of strokes, dementia and heart failure. The condition is the underlying cause of about 15 % of all cases of strokes (1). Today the risk of stroke is considered to be independent of whether the disease is permanent or paroxysmal, but it is low (1.3 % the next 15 years) in persons under the age of 60 with atrial fibrillation as the only risk factor for stroke (1).

«Physical activity» is a broad concept – it covers motion of the body at all levels of intensity and in all spheres of life (4). «Training» is defined as systematic, structured and repeated physical activity to achieve an improvement in physical fitness (4). Many studies concern athletes and atrial fibrillation of the paroxysmal type without other cardiovascular disease (5). People who train regularly typically suffer fibrillation attacks at night or after a meal, less frequently during the activity itself (5). This explains why those affected do not always associate their symptoms with training.

As everyday life and working life demand less and less physical activity, many people choose to get their exercise in the form of more intensive training. Many engage in interval training, aimed at increasing their maximum oxygen uptake capacity. It is also being tried out by groups with established risk factors for atrial fibrillation (6). The question of whether it is possible to «train oneself to fibrillation» therefore also applies to people other than those who engage in competitive sport, although the latter have been most in focus (2). Knowledge of a possible connection between physical activity and atrial fibrillation is also important to society, bearing in mind that even a slight increase in risk can have a major impact on morbidity if large sectors of the population are at risk. We therefore wanted to examine more closely the evidence base supporting the hypothesis that there is a relationship between physical training and atrial fibrillation.

Material and method.

We searched in PubMed on «atrial fibrillation» combined with each of the search phrases «physical activity», «endurance training», «physical exercise», «sport» and «athlete», and delimited it to the period 1995–March 2011. These search words led largely to the same articles – two review articles, a meta-analysis, a total of 17 individual studies and several commentary articles and letters to the editor. We included all individual studies and also recent review articles (2009–March 2011) with possible relevance for our problematisation. After at least two persons had read each article followed by a discussion, we excluded seven articles that were based on very limited data, including cross-section studies that may represent a selection of completely healthy elite athletes, and studies that we for other reasons decided were not designed to shed light on the relationship between physical activity and atrial fibrillation.

Results

Our searches showed that in the period 2009–March 2011, two literature studies (7, 8) and one meta-analysis had been published in which the prevalence of atrial fibrillation in people who trained was compared with the prevalence in various control groups (9). These articles all concluded that athletes and others who trained regularly ran a higher risk of atrial fibrillation. The meta-analysis yielded a total odds ratio (OR) of 5.3 (95 % confidence interval (CI) 3.6–7.9 (9). These three articles largely included the same original studies, including two that we excluded for methodological reasons. Our literature study covers ten studies. The main results of the seven most important studies are presented in tables, grouped according to design; the other studies are discussed in the text.

Table 1 (10, 11) shows age and gender, end-points and main findings of surveys of physical activity and atrial fibrillation in large cohort studies where there is wide variation in the physical activities of the subjects. One work, based on the Physicians' Health Study, included healthy male doctors aged 40–84 years (10). Validated questionnaires on both training and atrial fibrillation were used and the follow-up time was 12 years. The reference group consisted of the almost 40 % of the doctors who did not exercise regularly. The results for the age group under 50 showed that those who engaged in intensive training (which resulted in sweating) five to seven days a week ran a greater risk of atrial fibrillation (relative risk (RR) 1.7 (95 % CI 1.2–2.5)) than those where were inactive. There was little or no such tendency among the older participants. However there was a universal finding that jogging five to seven times a week was associated with a higher risk of atrial fibrillation (RR 1.5 (95 %) CI 1.1–2.1) compared with no intensive training. The risk to joggers increased with the distance they normally jogged. Conversely, there was no increased risk associated with intensive training in the form of swimming, cycling or tennis.

A cohort study based on virtually the whole population included elderly women and men (> 65 years, average age 73 years) drawn from Medicare lists (11). A total of 5 446 persons without atrial fibrillation were included. They had answered a Minnesota leisure time physical activity questionnaire, a validated questionnaire that includes intensity, frequency and duration of various types of physical activity. Calculated energy consumption is supplied for each level of physical activity. This varies from < 35 kcal/week for the least active to an average of > 1840 kcal/week for the most active. Atrial fibrillation was identified ten years later by means of electrocardiography and reviews of medical records. The lowest hazard ratio (HR), 0.7 % (95 % CI: 0.6–0.9) was found among those who took exercise in the form of walking at a moderate pace. The distance walked was inversely associated with risk. Those who engaged in more intense training came out approximately the same as the most sedentary. No effect modification was found due to gender, age or other heart disease (table 1).

A possible correlation between work-related physical activity and atrial fibrillation was investigated in a population-based Danish cohort study of men and women aged

Table 2 Physical activity and atrial fibrillation in patient-control studies

Study (first author, year)	Proportion of men (%)	Measure of physical activity	Odds ratio (OR) (95 % CI)
Elosua R, 2006 (13): Training for 51 patients < 65 years with lone atrial fibrillation vs 109 control persons from a health survey in the general population Atrial fibrillation identified at clinic	100	Questionnaire on current and previous physical activity	OR 2.9 (1.2–6–9) for lone atrial fibrillation with current sporting activity (at least twice and at least 2 hours/week) and total of > 1 500 hours of sporting activity throughout lifetime vs non-active now and totally active < 1 500 hours
Mont L, 2008 (14): Training for 107 patients < 65 years with lone atrial fibrillation vs 107 healthy family members Atrial fibrillation identified at Acute Admissions	69	Questionnaire on previous physical activity at work and leisure	OR 22.9 (4.3–121.2) with total moderately intensive physical activity ≥ 6 626 hours versus 0–138 hours, OR 7.31 (2.3–22.9) with total intensive physical activity ≥ 564 hours versus no intensive physical activity

50–65 years (12). The cohort was followed for 5.7 years on average, and atrial fibrillation was identified from a patient register. No increased risk of atrial fibrillation was found for «light standing or walking work», «work that requires carrying light objects and walking a lot, also on stairs», or «heavy physical labour», as compared to sedentary work (not shown in the table).

Table 2 (13, 14) shows the main results of the two studies with a patient-control design. A Spanish study covered 51 men with atrial fibrillation via a review of medical records at an arrhythmia clinic (13). The men were less than 65 years old, and 43 on average. Their physical activity was compared with the activity of 109 control persons from the general population by means of a non-validated questionnaire on current and earlier physical activity through their lives. The analyses were controlled for age, hypertension and height. The authors suggest a possible threshold value for the development of atrial fibrillation of around 1 500 hours of training in a lifetime (table 2).

Another patient-control study recruited 107 patients with lone atrial fibrillation with a duration of < 48 hours for the attack in question and an age of < 65 years (average 48 years) from Acute Admissions (14). Their level of physical activity was compared with that of 107 healthy volunteer control persons recruited among their relatives and visitors. Physical activity was measured by means of a questionnaire that covered work and leisure time, training intensity and physical activity back in time through their lives. The patients proved to have a substantially higher number of hours of moderate and high intensity physical activity, particularly in their leisure time.

Table 3 (15–17) shows studies illustrating the prevalence of atrial fibrillation among athletes who compete at elite level. One study included 262 male orientation runners (15). They were compared with men of the same age who were found fit for military service. The follow-up time was ten years. Overall, 14 orientation runners developed atrial fibrillation. The prevalence was 4.2 % in the age group 46–54, 5.6 % in the age group 55–62 and 6.6 % in the age group 63–70. The runners had a higher risk of AF than the recruits (OR 5.5: 95 % CI: 1.3–24.4). On average the runners with AF trained regularly for 36 years, and their first attacks came at the age of about 52 years (15). However, the orientation runners had a lower death rate than the control group (1.7 % versus 8.5 %) and lower incidence of coronary heart disease in the follow-up time (15).

After 28–30 years of follow up of 78 men who achieved repeated good results for the gruelling Birkebeiner ski run, Grimsmo et al. found 11 cases of AF, of which ten were «lone» cases (16). The age spread for the follow-up in this study was 54–92 years. On the other hand, Bjørnstad et al. found no cases of AF among 30 former elite athletes in the sports of cross-country skiing, biathlon, long-distance running, cross-country running and orientation after 14–15 years of follow-up (18). These athletes, aged 39 on average at the time of follow-up, had changed their exercise habits after completing their sporting career 5–12 years before the survey, but it is not clear how much and how intensively they had exercised in recent years.

Table 3 Studies of prevalence of atrial fibrillation in male athletes

Study (first author, year)	Type of physical activity	AF (n)[1]	Risk estimate (95 % CI)
Karjalainen J, 1998 (15): Cohort of 262 sportsmen compared with recruits, followed for 10 years Atrial fibrillation identified through questionnaire	Orientation, elite level for many years	14	OR 5.5 (1.3–24.4) for atrial fibrillation in sportsmen vs recruits
Grimsmo J, 2010 (16): Cohort of 78 «birkerbeiner» skiers followed from 1976–1981 to 2004–2006 AF identified by clinical examination, ECG and echocardiography	Skiing, high level of exercise for many years	11	12.8 % (n = 10) had atrial fibrillation without other cardiovascular disease
Molina L, 2008 (17): Retrospective cohort, 252 male runners compared with 305 sedate men from general population followed for 11.6 and 6.4 years, respectively AF identified by clinical examination, ECG and echocardiography	Marathon at exercise level	9	HR 8.8 (1.3–61.3) for AF in runners vs sedentary, adjusted for age and blood pressure

[1] No. of cases among athletes

A Spanish study compared the prevalence of AF in 252 male marathon runners (average age 39 years) and 305 sedentary men (average age 50 years) recruited from the general population (17). They responded to a validated version of the Minnesota leisure-time physical activity questionnaire. The marathon runners were followed for an average of 11.6 years, the control group for 6.4 years. There was an incidence of 11 cases of paroxysmal or persistent lone AF, of which nine cases among the runners and two in the control group (17). In material consisting of 62 former professional cyclists (average age 66 years), the prevalence of AF was found to exceed that among 62 golf players of the same age (19). In this study, the participants were asked about the use of performance-enhancing medical products, which 44 of the 62 cyclists had used, most commonly in the form of amphetamines or anabolic steroids.

Discussion

The conclusion of most of the studies we have reviewed gives the impression that intensive endurance training through several decades increases the risk of AF, at least in men over the age of 40. None of the studies that include less intensive exercise, such as walking, indicate that this increases risk. Can we trust these results?

Sources of error that must be taken into consideration

All the studies cited are observation studies. This implies at least three sources of error: selection bias, information bias and occurrence of confounding factors. Selection on the basis of age, which implies both biological aging, total exposure to physical activity and total exposure to other risk factors for atrial fibrillation, will be important in studies of AF. A high lower age limit for inclusion, as in the study based on the Medicare lists (11), may mean that a number of persons with training-related atrial fibrillation were excluded as already having cardiovascular disease at the time when subjects were being included in the study, so that there is a «healthy worker» effect. Those who have AF or similar symptoms may also have stopped training before inclusion. The fact that Bjørnstad et al. found no cases of AF in a study with an average age of 39 at the end of the follow-up time (18) may be due to chance or to the young age of the participants.

The over 16 000 participants in the Physicians' Health Study (10) were drawn from an initial population of over 200 000 doctors. As a general rule, selection processes do not necessarily affect effect estimates, but in this study we do not know whether the dropout rate was selective with respect to physical activity or AF. Studies based on clinical material are subject to selection bias because it is not chance that determines which patients are evaluated at the individual clinic (13, 14). In a number of studies, it is also conceivable that there is selection bias in the control groups (13–15, 17, 19).

There is a high risk of information bias if the registration of the end-point (here AF) is associated with the exposure that is being studied. In retrospective patient-control studies (13, 14) it is possible that persons with AF remember their training in the course of the years better than healthy control persons do. This can have a pronounced effect when one asks about training going far back in time, as was the case in these studies (13, 14. The question of whether there is information bias is particularly relevant when family members are used as control persons (14). It is also possible that those who train hard are particularly body conscious and troubled by symptoms and will therefore be particularly inclined to ask for help and have atrial fibrillation recorded. However, it is also possible that these particular people avoid going to a doctor in order to avoid the stamp of disease and medication, particularly in the case of rare attacks and not very troublesome atrial fibrillation, and choose rather to reduce the amount and intensity of their training.

In observation studies efforts are made to control for confounding factors: in this case, that physical activity may be associated with other factors that may influence the risk of AF independently of physical activity. Other cardiovascular disease, diabetes, overweight and metabolic disorders may have an effect (most frequently inhibit) physical activity and in themselves increase the risk of the disorder (1). Particularly in elderly people, this could contribute to a negative correlation between physical activity and AF. A number of the studies we reviewed included a clinical examination and may have a sound control for disease, while others are based solely on self-reporting of disease (10, 12) or lack information (15).

Height and body-mass index (14, 20) and also regular alcohol intake (21) are now established risk factors for AF. In a meta-analysis of 14 studies, it was found that alcohol consumption in particular is associated with paroxysmal lone AF, and the results indicated a gradual increase in risk from relatively low daily intake of alcohol (21). Of the studies we have reviewed, only the large cohort studies (10–12) and the Spanish study of marathon runners (17) contain systematic information on these factors. In other studies, the information on possible confounding factors is sparse or non-existent (14, 15), and some studies also had other methodological weaknesses (13, 14, 17, 19).

The importance of performance-enhancing medical products as a cause of AF is insufficiently known (1). It is possible that physiological levels and low-dose testosterone supplements have a protective effect, whereas anabolic steroids in large doses appear to increase risk (22). There was information on the use of anabolic steroids in one of the studies we reviewed (19), but we have not found studies where it has been possible to control for this information in the analysis.

Inflammation – link in a causal chain?

A possible explanation is that a correlation between training and AF is due to the combined effect of increased sympaticus tone and volume loading on the heart during the activity itself, increased vagus tone at rest and structural changes such as hypertrophy and dilatation (1). It is conceivable that myocarditis and pericarditis increase the risk of AF directly by causing structural changes while the infection is in progress and by autoimmune reaction subsequently (23). Those who train a lot may be particularly susceptible to infections that affect the circulation organs, and they may also train while they have an infection. A correlation has been found between inflammation markers in blood and the prevalence of AF after 14 years of follow-up (24), and this may provide backing for an inflammation hypothesis. However, it has also been found that moderate physical training can reverse inflammation in elderly people (25).

Conclusion

It has been convincingly documented that regular physical activity, not least intensive endurance training, prevents early death (26) and coronary heart disease (26, 27). However, this literature study provides support for the hypothesis that intensive endurance training for many years may increase the risk of AF. No studies to date have found signs that less intensive physical activity increases the risk.

A number of the studies we have included have methodological weaknesses, however, and the results must be interpreted with caution. Two review articles (7, 9) included two studies based on the same material: 51 men with lone AF (our reference 13, and an older study not included by us). This may be an example of a field of research being pushed towards publication bias and overestimation of the relationship being studied (28). Moreover, the studies we have reviewed are not directly comparable because they vary in their definition of physical activity and AF. There is also a wide age variation.

Most of the study participants are men, and there is no basis for reaching any conclusion concerning the effect of physical training on the development of AF in women. The number of women who train may have been too low in the studies conducted up to the present. There is a need for follow-up studies that include young people, so that potential differences by age can be studied. In further studies intended to shed light on a possible correlation between physical activity and atrial fibrillation, more attention should be paid to training frequency, duration, intensity, and the combined volume of training.

We do not know whether high-intensity

interval training of short duration entails a higher risk than longer-term training with lower intensity and a larger combined training volume. The study that indicates a threshold level of 1 500 hours of intensive training during a lifetime, equivalent to two hours a week for 15 years, should be followed up by larger and methodologically stronger studies. There should also be focus on genetic vulnerability, and it is important to control for risk factors other than physical activity such as height, body mass index, alcohol consumption, metabolic disease, high blood pressure and other cardiovascular disease. And – perhaps most important of all – women must be included.

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