Endurance sport and cardiac injury

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INTRODUCTION

The possibility of myocardial damage by physical activity has been known about since ancient times. According to the legend, a soldier named Pheidippides (more likely Philippides) dropped dead after running to Athens from the battle at Marathon with the news of victory [1]. Whether he was a soldier or a courier, having already done 240 km from Athens to Sparta and then back, passing Marathon to Athens, and what finally is truth and what is fiction remains unknown [2]. What is clear, however, is that this death has gone down in history as the first sport-related death.

The probability of sudden death in connection with sporting activity is about 4.6/10,000,000/year in an average population (France). Some 6% of this cohort comprises young athletes [3]. Sudden cardiac death (SCD) is a rare event in the case of a young athlete (2.3 in 100,000 per year) [4]. SCD in general has an incidence of 0.36 to 1.28/1,000/year in the industrialised world [5]. And these are only the data of individuals who have been resuscitated. The number of unreported cases is much higher. So sudden death in connection with sporting activity occurs only rarely. However, because it affects people who are believed to be healthy, the effect is more spectacular and when such an event occurs, especially during professional football, there is great media hype.

Physical inactivity is thought to be responsible in up to 25% of all cases for the development of breast- and colorectal cancer, up to 27% for the development of diabetes mellitus, and up to 30% for the development of ischaemic coronary heart disease (CHD) [6].

The published reports referring to the risk of SCD [3, 7, 8] as a result of sport are uncertain, in spite of the many known positive effects on the survival rate [9]. Endurance athletes — amateurs as well as professionals — are concerned about the spectacular sudden deaths during a marathon [10] and triathlon [11]. Not only the general population but also physicians feel insecure because of reports about injury of the left ventricle (LV) [12–15] and right ventricle (RV) [16–19]. Overall all-cause mortality of professional endurance athletes is reduced [20–23]. In the case of a hobby-athlete, the prognosis seems not to depend on the sporting activity but on the individual risk constellation of the athlete [24]. Due to the very different-seeming reports, it is necessary to critically discuss the studies referring to the negative effects of endurance sport and its impact on cardiac injury ('cardiac fatigue' [25]) and SCD. Figure 1 illustrates possible factors that might affect the myocardial function of athletes.

PATHOPHYSIOLOGY OF ENDURANCE PERFORMANCE

Different changes of the cardiac structures may occur as consequences of chronic 'bouts' of vigorous exercise [26–28].
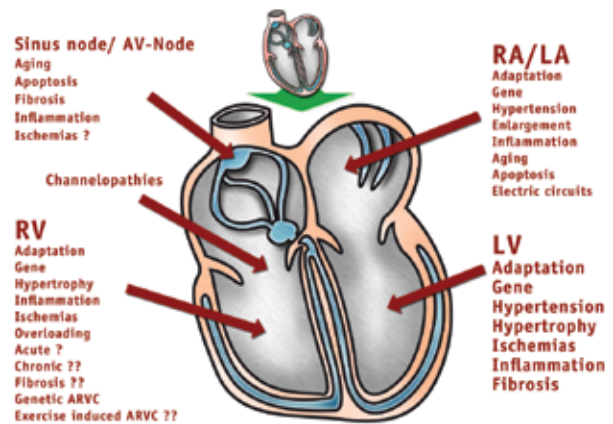

Figure 1. Possible factors that might affect cardiac function in athletes; AV — atrioventricular; ARVC — arrhythmogenic right ventricular cardiomyopathy; LA — left atrium; LV — left ventricle; RA — right atrium; RV — right ventricle

The adaptation of the heart to greater strain is a well-known phenomenon [29–31] and was first mentioned by Henschen, a Finnish physician, at the end of the 19th century [32]. The physiological modification of the heart is a 'harmonious increase in size' and myocardial hypertrophy of the healthy heart, caused by physical activity [33]. The influencing factors are the kind of physical activity on the one hand, and individual disposition and environmental effects on the other. Morganroth et al. [34] described, in simplified terms, that endurance performance would mainly represent a kind of volume overload; the result is an eccentric hypertrophy. However, strength endurance training is more likely to cause a concentric hypertrophy. But today there are different types of athletic heart and the formula of Morganroth is not necessarily straightforward to transfer to sports disciplines [30]. The probability of the negative role of hypertrophy in athletes [35] and the problem of qualitative and quantitative relevance are under discussion [36, 37].

The influence of different clinical variables on the LV size of an athlete's heart is considered up to 50% as influence of the body surface [38]. Additional factors are up to 15% the sport, up to 7% the gender, and up to 4% the age. The influence of other factors (of an individual kind) is estimated as 25%.

The so-called athlete's heart is characterised by numerous changes in electrocardiogram (ECG). 40% of athletes show abnormalities in their ECG [38, 39].

The frequency of the changes in ECG depends on the kind and intensity of training and on the sport. Mainly changes like extended QRS-complexes, diffuse modifications in T-waves, deep Q-waves or even 'bizarre' ECGs have been recorded [38, 40].

The cardiac response to overload can be seen as a complex process; it depends on different variables such as heart-rate, pre- and afterload of the ventricle, LV and RV end-diastolic and end-systolic volume, as well as the neurohumoural situation [26, 27, 41]. Changes of the preload of an athlete depend on shifts in volume, for example by sweating or by increased fluid intake, the afterload for example by heat build-up or vasodilatation [42–44]. More changes occur on a cellular level by acidosis [45], withdrawal of glycogen [46] or oxidation [47]. Oxidative physical stress has been proven in animal experiments [48].

The morphologic changes after high stress, as reported by King and Gollnik [49], can perhaps be interpreted as a shift of the balance of intramyocardial calciumiones (Ca^{2+}). There have been similar observations in the case of chronic hypoxia [50]. This situation can be altered by training, at least in the case of rats, so that the effects of hypoxia and the negative impacts can be repealed [51]. Benito et al. [52] were able to show by experiments with rats how intensive training induces fibrosis of the RV, including an increase of transforming growth factor-beta1 also in the right and left atrium (potent stimulator of collagen producing myofibroblasts). Fibrosis was seen as a promotor of electrical heterogeneity and arrhythmogenesis,

at least in the case of atrial fibrillation (AF) [53]. The underlying mechanisms, however, are far from being clarified: extent of fibrosis and AF, lack of AF in case of other major changes like amyloidosis/haemochromatosis [53].

It is unclear to what extent these results concretely can be transferred to the advanced human heart. Animals were treated in part with electro-shocks [52] and this stress factor cannot be compared to a well-trained, voluntarily acting athlete. We cannot completely ignore those indications for a cellular and structural remodelling in animal testing, however, the evidence of complete transferability to the human heart is still lacking.

The possibility of the development of myocardial fibrosis in an athlete's heart exists. To date, it has been shown in two (post mortem) cases of former athletes who died, mainly in the LV [54, 55]. Furthermore it is proven by magnetic resonance imaging (MRI) [19, 56, 57].

For further evaluation there is a need for prospective studies. All studies which examine endurance sport are required to take the kind, intensity, duration and environmental situation (i.e. weather, humidity, temperature, wind speed) of the action into account. Moreover, before, during and after exercise as many additional parameters as possible should be collected (e.g. liquid and calories intake, weight, pH-values).

SUDDEN CARDIAC DEATH AND SPORT

SCD in the case of a young athlete is, with an incidence of 1:160,000/person/years [4], a rare and unexpected, but always tragic, event.

In the United States, 50–75 deaths per year occur in young athletes, and in France about 10–15 [3].

Marijon et al. [3] describe the common risk of SCD in connection with sport with 5.4 up to 16.7/1,000,000/year — depending on the region. The mean age of the persons concerned was 46 ± 15 (11–75) years, 92% died directly during sport, only 12.7% had disorders before and 86.5% had had regular training. SCD occurred in young athletes with a frequency of 9.8/1,000,000/year, in young non-athletes 2.2/1,000,000/year. Among the general population, the risk is about 9.2/1,000,000/year for men and 0.4/1,000,000/year for women. So young competitive athletes have a five-fold higher risk than non-competitive athletes, and men have a 20-fold higher risk than women.

Most deaths concerning young athletes occur during or soon after sports activity. Literature differentiates between 'young' and 'old' athletes (< 35 and > 35 years). So far, depending on age and country, there have been significant differences in screening [4, 7]. Besides recommendations on a medical basis, also aspects of national and economic concepts have to be discussed. Discrepancies derive in part from the different country-specific views to assess SCD in the case of an athlete < 35 years. Potential causes of SCD are shown in Table 1. More attention should be paid to the variety of

Table 1. Causes of sudden death in young athletes aged 12–35 years

Cause of sudden death	Maron et al., 2007 [7] (n = 1,049)	Corrado et al., 2003 [4] (n = 55)	Solberg et al., 2010 [8] (n = 22)	Marijon et al., 2011 [3] (n = 50)
Aortic rupture	2.2%	1.8%	4.3%	2%
Aortic stenosis/congestive heart disease	1.8%		4.3%	6%
Arrhythmogenic right ventricular cardiomyopathy	4%	22%		4%
Channelopathies (QT, WPW)	3%	1.8%	8.7%	12%
Coronary artery anomalies	24%	11%	3.3%	
Coronary disease	3%	18%	48%	6%
Dilatative cardiomyopathy	2%	1.8%		4%
Hypertrophic cardiomyopathy	36%	1.8%	4.3%	10%
Mitral valve prolaps	4%	7.3%		2%
Myocarditis	5.4%	9%	22%	4%
Possible hypertrophic cardiomyopathy	11.3%			4%
Riva muscle bridge	2.2%	3.6%		2%
Unclear		1.8%		36%

causes than to the absolute figures, which vary widely over the years among the authors.

In their most recent publication, Maron et al. [7] see hypertrophic cardiomyopathy in 36% as the cause of SCD.

In their update from 2006, Corrado et al. [58] regard a silent CHD in young non-athletes as a determining cause of sudden death. Physical exercise in the case of young athletes < 35 years is not per se associated with risk, but depends on a possible individual and silent disposition. This may be for example hypertrophy, CHD or arrhythmogenic disposition and can be triggered by physical exercise. Above all, what is important is not the knowledge of percentage rates mentioned in the literature, but the variety of findings and possibilities, which cannot be diagnosed by simple 12-channel-ECG.

The situation among those active beyond 35 years old is quite different. The primary cause for sudden death is almost always CHD [59]. General recommendations to identify persons at risk are available [60, 61].

Analysing the literature regarding the recommendations for screening, the options may be as follows: on the basis of the Italian criteria, mainly medical history, physical examination and 12-channel-ECG are recommended: in accordance with the American criteria, medical history and physical examination are sufficient; in the case of any abnormal findings, imaging techniques, exercise test and Holter-ECG should be carried out.

Nowadays these recommendations should be regarded as a minimum, with increasing importance of echocardiography [62, 63] and MRI [57, 64] examination.

However, CHD is relatively common in young athletes < 35 years [8], so younger athletes should also undergo exercise tests.

In the case of abnormal ECG-findings, a stress echocardiography should be carried out [62, 63]. Athletes over 35 years of age, undergoing an extreme endurance competition, for example triathlon or marathon, should be examined by stress echocardiography from a prognostic point of view [63]. Competitive ambitious athletes < 35 years should undergo a specific cardiologic examination and regular annual check-up examinations, if problems occur and before starting training. When myocarditis or RV dysplasia is suspected, cardio-MRI examination should be performed to confirm or exclude the diagnosis [57, 64]. The diagnosis of possible 'fibrosis' should be considered in specific clinical situations.

The cost-benefit ratio of a combined exercise-ECG and echocardiography or spiroergometry and echocardiography in terms of the costs of an ambitious physical exercise is acceptable. The costs for screening-examinations should be regarded as negligible given the high expenditures for preparation and participation in marathon- and triathlon competitions [65]. The recommendations about athlete screening are under discussion [66].

RIGHT-VENTRICULAR INJURY BY SPORT

The description of acute deaths relating to arrhythmogenic right ventricular cardiomyopathy (ARVC) is based on the publication of Thiene et al. [67]. In 12 of 56 acute cardiac deaths, ARVC was diagnosed (athletes < 35 years). This has never been confirmed to this extent by another working group. In 2007 Maron et al. [7] found the figure to be 4% and Marijon et al. [3] in 2012 found it to be 1.4%.

Heidbüchel et al. [17] postulates the term 'load induced, right-ventricular arrhythmogenic cardiomyopathy' that could lead from repetitive microtraumas to chronic and structural

changes of the RV and to 'pro-arrhythmogenesis'. In his view, ventricular tachycardia originating from the RV is responsible for the acute deaths. His hypothesis is based on a retrospective analysis of electrophysiological examinations in 2003 [16]. A cohort of only 46 athletes from three centres was analysed retrospectively — without further details on period or overall cohort. In 28/46 cases, a MRI-examination was carried out, in 12 cases with abnormal findings of the RV (hypokinesia, dilatation or fat tissue). The entire theory is based on these cases. Unfortunately, statements concerning the prevalence or incidence of a remodelling of the RV among athletes are not possible, because of the lack of information for the necessary statistical values. Also the number of cases is extremely low.

In 2012, LaGerche et al. [19] reported a structural remodelling of the RV among 40 endurance athletes from different disciplines that are in part not comparable with respect to disciplines, intensity and mode of exercise. In 2008 [68], based on a study similar in design with 20 male and seven female triathletes, they also reported LV and RV dysfunction among participants of the Australian Ironman competition performed in 2004 (3.8 km swim, 180 km cycle, 42,195 km run).

As regards trials in the United States [7] and France [3], a participation of the RV as cause for SCD has rarely been demonstrated.

RV remodelling should also have been described by the echocardiographic examinations of Maron et al. [69] (screening of 4,111 young athletes). The statements by LaGerche et al. [19] based on 40 athletes are rather problematic, because Basavarajaiah et al. [70] described no abnormal findings of the RV in their examination of 3,500 athletes, and the same applies to the cohort of Maron et al. [69] with 4,111 athletes. In the small cohorts of Heidbüchel et al. [16] and LaGerche et al. [19], those changes occur frequently. These findings give some cause for scepticism. We have to differentiate between acute and chronic changes in the RV function induced by exercise. La Gerche et al. [19], described in 2012 an acute change in RV function and Heidbüchel at al. [16] described in 2003 a chronic change of RV anatomy induced by exercise.

A correct quantitative assessment of the RV volume is made difficult or impossible because of the possibility of different ultrasound angles and individual anatomic geometry [71, 72]. Conventional quantitative assessment of RV using two dimensional (2D)-echocardiography is limited by asymmetric and complex pyramidal shape of RV [72, 73]. Interobserver variability to determine the volume of the RV can be as much as up to 16% using MRI [74]. The interobserver variability as well as the day-to-day variability in the study of LaGerche et al. [19] remains unknown. An interobserver variability of between 10% and 15% could be expected. A 'post-race' increase in volume of the RV of 9 mL (5% of 170 ± 30 mL) is very small and well below interobserver variability. It is questionable whether we can call this difference clinically relevant. However, this change cannot be uncritically accepted as an 'injury-theory' of the RV that would be valid for all endurance athletes.

The shifts in plasma and volume under endurance exercise have a significant influence on cardiac function [27, 44]. These changes (weight/fluid intake) have not been adequately described and documented in the study of LaGerche et al. [19]. It is also unclear why the RV mass, which only amounts to 25% of the LV mass, should be responsible for the increase of bio-markers and not the LV or rather the massive degradation of the muscle.

A further problem concerning this study is the lack of documentation about cohorts, time-periods and races. A balancing act, concerning participants across all disciplines and distances, is problematic in any case considering such an important phenomenon.

Also long term trained marathon runners have not been shown to suffer any long term injury of the RV (incl. strain-technology) [75]. D'Andrea et al. [73] examined 650 leading athletes and described signs of adaptation of the RV to exercise. Signs of fibrosis or RV cardiomyopathy were not reported. These findings of RV enlargement (adaptation) require follow-up investigations in the future [73].

Accordingly, before any further extension of the 'exercise-induced RV fatigue/fibrosis' hypothesis, further prospective studies on this issue are recommended. We have to estimate a possible prevalence and incidence in the future. Both data are not known. The hypothesis has interesting aspects, but the dose of the exercise bouts has to be evaluated and the individual phenotype [76], environment [44] or inflammation [77] and oxidative stress [78, 79] dependency has to be regarded. In all studies, an accurate monitoring of liquid intake before, during and after the competition, incl. weight measurements, should be carried out as well as precisely documented courses of calorie intake, because also loss of glycogen of the myocardium may cause fatal consequences [46] and preload conditions may affect the results [80–82].

LEFT VENTRICULAR DYSFUNCTION, INCREASE IN BIO-MARKERS IN COMBINATION WITH MRI

Numerous investigations regarding the increase in bio-markers (mainly troponin [cTnI] and NT-proBNP) in marathon [15, 83] as well as in triathlon [14, 68] competitors have been conducted. A significant increase in bio-markers after the race has been found in all these studies. At first, uniformly, the increase of biomarkers was considered as proof of a possible injury of the heart muscle [14, 84, 85], but more recently it has been seen rather as a physiologic response to exercise [86]. The intensive consideration of cardiac dysfunction after physical exertion (often called 'cardiac fatigue' [25]) has mainly been pushed forward by observations in marathons and triathlons (ironman: 3.8 km swimming, 180 km cycling and 42,125 km running races). Also deaths during marathon

competitions [87] have boosted the idea of cardiac injury by endurance competitions.

In addition, numerous studies using imaging techniques in marathons as well as in triathlons have been conducted. The studies of Neilan et al. [15] and Möhlenkamp et al. [88], have been the source of very controversial discussions [89, 90].

Tulloh et al. [84] reported in 2006 a decrease of the ejection fraction from 64.2% to 58.6% with a simultaneous rise in cardiac output from 6.66 l/min to 7.23 l/min. There was no documentation of shifts in volume or weight before or after the race, respectively. Accordingly, the findings are difficult to interpret. The changes in the cardiovascular system after an ironman competition are so significant that an analysis about a systolic LV injury is not possible based on the presented data. Neilan et al. [15] found no significant changes of the systolic function or dimensions of the LV after the marathon at all, but an alteration of the diastolic function of the RV and LV. These changes, combined with the increase in bio-markers, were judged to be a sign of myocardial injury with consecutive increase in pulmonary pressure and RV enlargement. The end-diastolic RV area was 17 ± 4 cm^2 before the race and 20 ± 3 cm^2 after the race. Weight and liquid intake were not documented, and lactate values were not measured. Considering the minimal echocardiographic changes and massive changes of the cardiovascular system due to competition at the same time, the evaluation of the results of the study as myocardial injury is highly questionable. The overall constellation, incl. the increase of bio-markers, is not convincing and doesn't underline LV injury necessarily.

Biochemical and functional abnormalities have also been reported by LaGerche et al. (Ironman Australia 2004) [68]. Here was a decrease in LV ejection fraction after the ironman competition from 60.4% to 57.5% (p-values not given). There was only a significant increase in bio-markers in two athletes out of 27; these cases were however significant, with a remarkable impact on the statistical values.

Overall, the increase in bio-markers in athletes with intensive muscle work should not necessarily be interpreted as heart-specific [91], because it also depends on the athlete's weight [92]. So there is still the option of loss in specificity of the assays, when such a high muscular destruction has occurred (possible increase in CK up to 10,000 U/L). The assays have not been developed for this massive muscular destruction.

MRI can visualise myocardial scars, but any clear evidence for de novo scarring directly after competitions is still pending [93].

COMPETITIVE/AMBITIOUS ENDURANCE SPORT AND POSITIVE OR NEGATIVE EFFECTS

Generally, endurance athletes live longer compared to the general population (Table 2). Female athletes seem less frequently to suffer damage by endurance sport than do males [94, 95]. In some cases (genetic aetiology/channelopathies) and individual situations (infections/inflammations), life expectancy can be shorter [54, 55, 77]. The study by Marijon et al. [22] reports positive effects of professional endurance sport. Professional cyclists presented 41% lower all-cause mortality than the general population (Table 2). Also the current meta-analysis by Teramoto and Bungum [96] reports a lower mortality (especially cardiovascular) and a longer lifespan of elite athletes. Of course, these results have to be interpreted with caution. Lifestyle and genetic predisposition may be more advantageous than the variables in the general population. The investigation of 2,613 male elite athletes by Sarna et al. [97] also showed an increase in life-expectancy of endurance athletes compared to the control group (75.6 vs. 69.0 years).

A long-term analysis of the standardised mortality ratio of athletes between 1924 and 2000 from Poland showed a clearly longer life expectancy of male athletes (Olympic athletes) [20].

Athletes with intensive cardiovascular training in their disciplines have shown a slight decrease in mortality [98].

Similar results were obtained by two other studies investigating prospective not professional, but ambitious and semi-professional athletes. The Swedish study of Farahmand et al. [99] examined 73,622 participants of the traditional Vasa cross-country skiing across 90 km and 30 km. The reduction of total deaths was 52% compared to the general population. In a second study, 2,259 male Dutch skaters [100] having participated in a race across 11 towns in 1956 were followed-up after 32 years. They were divided into the group of competitors (259) and into the group of hobby-athletes (2,000). The reduction of mortality was only seen in the group of ambitious athletes. Here total mortality was reduced by 24%. However, among the over 50-year-old athletes, there was no significant difference compared to the general population regarding the survival rate.

On average, joggers live 6.2 years longer than non-joggers (women 5.6 years) [23].

Ambitious sporting activity, up to 6,300 kJ/week and more, showed a reduction of mortality with increasing physical activity in the Harvard Alumni Health study [101].

The follow-up analyses of top athletes practicing their sport for up to 17 years showed no cardiac damage [102]. Pelliccia et al. [102] examined 114 Olympic athletes (48% canoeists, 17% cyclists, 15% middle- and long-distance runners, 13% cross-country skiers, 5% middle-distance swimmers and 2% triathletes). None of them showed signs of left cardiac damage, even though all athletes trained at the highest level.

How intensive the training should be to achieve a positive effect on life expectancy is unclear [103]. Perhaps it corresponds to the approximated calorie consumption of 490 kcal/day derived from evolution [104]. But even physical activity up to 1,000 kcal/week reduces the mortality rate by up to 30% [9]. There is also a positive relation between intensity of training and general survival rate [105]. Those over

Table 2. Longevity/mortality in athletes

Author/kind of athletes	N	Years	Age [year] (longevity)/SMR/OR (mortality)	
Sarna, 1993 Finnish Word Class	2,613 M	1920–1965	75.7 — endurance sport	
			73.9 — team sport	
			71.5 — contact sport	
			69.0 — reference	
Gajewski, 2007 Poland Olympics	1,689 M	1946–2000	0.50 — athletes	SMR
			0.78 — actors	
			0.64 — monks	
Karvonen, 1974 Endurance Skiers	396 M	1893–1967	73.0 — all	
			70.2 (1950–1967) — controls	
			68.7 (1946–1950) — controls	
			68.9 (1931–1935) — controls	
Saase, 1990 Ice Skating Tour	259 M	1956–1988	0.59 — non-elite racer	SMR
			0.72 — 'elite' participants	
			0.80 — 'non-elite' participants	
			0.90 — racer	
Zwiers, 2012 Netherlands Olympics	9,889 M	1896–2011	1.01 — cardiovasc moderate	Mortality
			0.98 — cardiovasc high intensity	
			0.94 — moderate static	
			0.99 — high static	
			0.94 — moderate dynamic	
			0.97 — high dynamic	
Marijon, 2013 Tour de France	786 M	1947–2012	1.65 — controls	SMR
			0.56 (1947–1970) — cyclists	
			0.54 (1971–1990) — cyclists	
			0.62 (1991–2010) — cyclists	
Farahmand, 2003 Valsoppet Ski Race	49,219 M	1989–1998	0.72 (100–120% winner time)	SMR
			0.53 (121–160% winner time)	
			0.47 (161–200% winner time)	
			0.49 (201–240% winner time)	
			0.48 (> 240% winner time)	
			0.32 — successful in all six races	
Schnohr, 2012 'Joggers'	1,878 M + F	1976–2003	6.2 > controls men	
			5.6 > controls women	

OR — odds ratio; SMR — standard mortality ratio; F — female; M — male

45 years should train daily (30–60 min) in a moderate way (41 METs hour/day) [106]. Higher physical efforts would have no sure advantage regarding the survival rate, and perhaps even negative effects [106].

There is no doubt that athletes have a higher incidence of AF and bradyarrhythmias in aged athletes [107, 108]. The relevance of possible fibrosis of the left atrium [53], exercise-induced hypertension [109] (Fig. 2) or other causes [110, 111] remains open. Figure 3 shows the onset of AF in a 51-year-old cyclist during exercise ECG with heart rate up to 230 bpm. Figure 4 shows slow recovery of deformation measured using strain-echocardiography after conversion from AF to sinus rhythm [112].

In the case of the 52,755 cross-country skiers of the Vasa-race [108], AF and bradyarrhythmias occurred more frequently (14.3/10,000/patient/year and 1.9-2.8/10,000/patient/year). However, more frequent occurrence of supraventricular/ventricular tachycardia and cardiac arrest compared to the general population was not seen.

The general discussion of arrhythmias and sport remains controversial, because the causes and effects are still not clear at present (underlying disease, predisposition, training
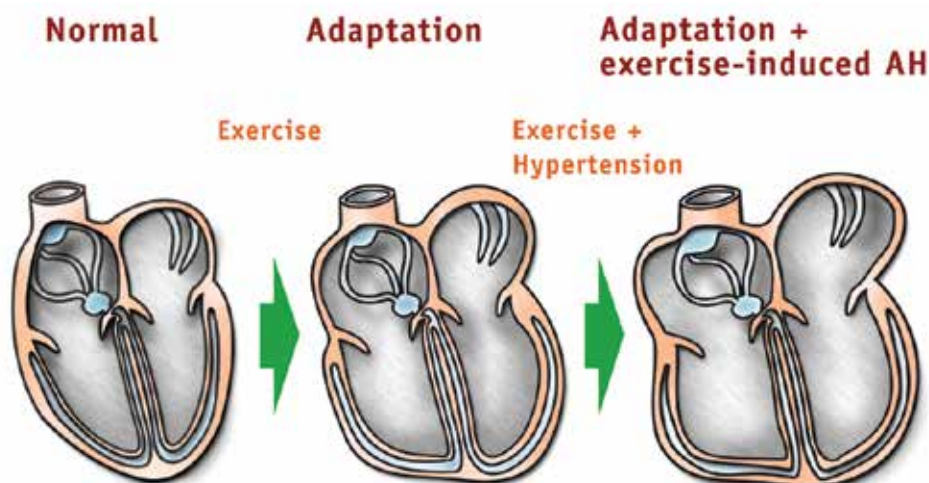
Figure 2. Possible effect of exercise-induced hypertension in endurance sport; AH — arterial hypertension
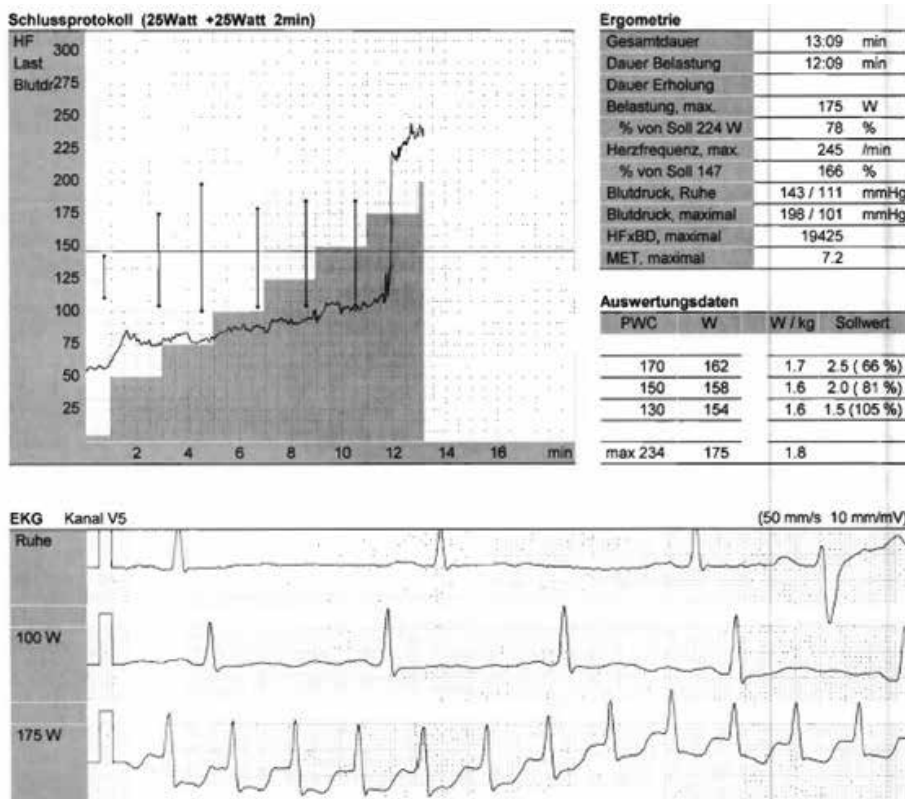

Figure 3. Atrial fibrillation during exercise in a 51-year-old cyclist

situation, circumstances). Sport itself is not arrhythmogenic. It needs perhaps a 'trigger-point': an inflammation, coronary disease, exercise-induced arterial hypertension (Fig. 2) [109] or genetic disposition [110].

The recent general reviews on the potential side effects of ambitious endurance sport have differing views. Scharhag et al. [113] came up with a thesis that ambitious endurance sport will not lead to myocardial damage or negative ef-

fects. O'Keefe et al. [114] agree with the statement that ambitious endurance athletes have lower mortality ratios, although they also suggest the hypothesis that excessive endurance training may lead to negative cardiovascular remodelling. To verify this hypothesis, a confirmatory longitudinal work is necessary. The latest publication of the Nixdorf-Recall study revealed that for older athletes (> 50 years), it is not the increase in troponin-markers during a marathon, but the
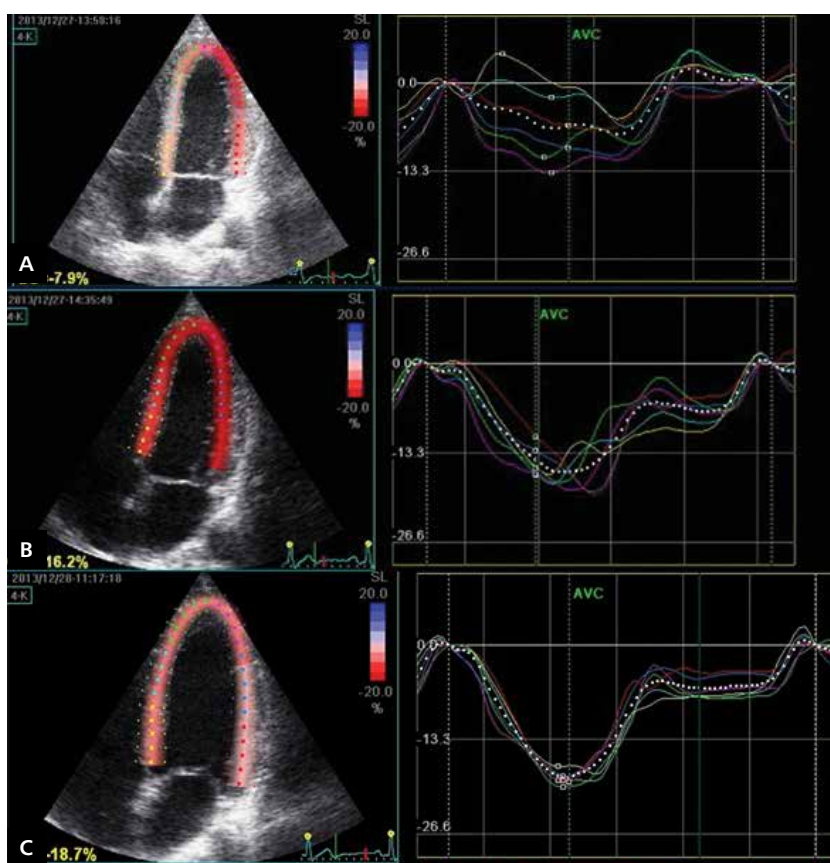
Figure 4. A case of atrial fibrillation (AF) in a 48-year-old cyclist and marathon runner. Left ventricular deformation measured by strain-echocardiography; **A**. During AF; **B**. Five minutes after conversion to sinus rhythm; **C**. 24 hours later

individual risk of cardiovascular disease that is of prognostic significance [24]. These studies indicate that endurance sport per se does not present a risk, but that 'individual burden of disease' determines the risk for mortality.

SUMMARY

Based on the studies discussed in this review, we can say that ambitious physical exercise can result in cardiovascular side effects in athletes < 35 years and > 35 years. In particular, a life-threatening complication may be caused by ischaemia, when CHD is not yet known. Also an unknown structural disease may be triggered negatively by massive physical load. Here, individual predisposition and genetics have to be considered [76, 115].

The studies carried out on the phenomenon known as 'negative right ventricular remodelling' are based on a very small number of cases [16, 19], compared to those studies not detecting any alterations of the RV [69, 70] (these two cited studies were not focused to the RV). Both studies into exercise-induced RV injury [16, 19] have shown fundamental methodical deficiencies. An impact of negative RV remodelling exists, but the frequency seems to be rarer than that suggested by Heidbüchel et al. [16, 17] or LaGerche et al. [19]. In

all cases, we have to differentiate between acute and chronic effects. The general incidence, the dose of exercise bouts, and individual sensitivity must be defined and evaluated by further prospective studies. There is a lack of information on prevalence and incidence, and the post mortem studies on SCD do not provide the expected and assumed frequency. Here as well, the theoretical model of cardiac remodelling cannot be transferred to all athletes. Although it is possible, it depends on genetics [115, 116], exercise-induced arterial hypertension [109, 117], or environmental influences (bacterial/viral/oxidative inflammation). An individual predisposition to premature fibrosis/remodelling may exist [55, 56] (more LV). Negative changes of cardiac structures may be triggered by exercise, although dose response relationship, extent, clinical relevance and frequency remain unclear. Referring to the anatomic post-mortem studies, ARVC-frequencies of 4–20% would be possible among < 35-year-old athletes.

Considering the dominant probability of CHD in ambitious athletes > 35 years, risk stratification with exercise-tests/imaging techniques is advisable, in addition to basic examination (medical history/physical examination/12-channel-ECG). Spiroergometry/lactate diagnostics are recommended to ensure predominantly aerobic training.

Marijon et al. [3] reported a five-fold higher cardiac mortality in young ambitious competitive athletes (relative risk 9.8, 95% CI 3.7–16) than in non-competitive athletes (relative risk 2.2, 95% CI 1.4–3.0). This fact supports the need for a more detailed examination of athletes < 35 years and to identify persons at risk.

For all athletes < 35 years, minimal screening by 12-channel-ECG is controversial [66] and basic examination prior to the start of training or if discomfort occurs are not sufficient, based on today's criteria, and should be complemented by echocardiography and exercise-test (ECG or stress-echocardiography). Depending on medical history, Holter-ECG (especially in older athletes [118]) or MRI scan may become necessary. MRI can provide additional information concerning possible myocarditis, AVRC or fibrosis of the myocardium [57, 64, 119]. Strain-echocardiography seems to be also very promising, but still has to be verified [61, 120].

In all athletes with suspicious inflammation/myocarditis or in cases of power/performance loss, blood tests must be performed (especially for *Chlamydia pneumonia*) [77] or other bacterial or viral infections.

Increased risk remains for arrhythmias (particularly AF) at an advanced age, but these are easily treatable [121]. Arrhythmias are declining by de-conditioning up to 90% [122]. In rare cases, a pacemaker implantation in nodal disease is required [123]. It is certain that elite athletes (particularly men) have a longer life because of the rare occurrence of cardiovascular diseases [20, 22, 96, 99]. Cases of early death in individual cases due by myocardial fibrosis are possible [54, 55]. Here LV fibrosis was seen more often. Regarding the results of longevity or mortality studies in athletes, it is not possible to say that 'the faster lives longer' (Table 2). The standard mortality ratios are lower for successful participants of all races and with a finishing time > 240% of the winner's time [99] and a 'non-elite' racer shows lower standard mortality ratios than an elite racer (Table 2) [124]. One of the best solutions in the elderly could be moderate sport activity over long periods of time.

Further prospective studies on possible cardiac 'negative remodelling' by sport ('exercise induced cardiac-fatigue') with larger cohorts and under clearly defined conditions should be conducted. In addition, the optimal training volume of physical activity concerning the general survival rate should be investigated prospectively.

Regarding all the competitive sporting activities with an enormous importance for hobby-athletes, media and industry, physical activity in the general population is of fundamental importance [6, 9, 125]. Here, an evolutionary perspective and a recommended calorie consumption of 490/kcal/day are very valuable [104].

Sport is of great social importance. Accordingly, preventing sudden sport-related deaths or a 'negative remodelling' by sport has not only an individual component, but also a significant social impact on physical activity in the general population. In this regard, further studies in the industrialised world are socially justified and financially reasonable.

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