Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 44, No. 1, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.02.057

Serial Left Ventricular Adaptations in World-Class Professional Cyclists

Implications for Disease Screening and Follow-Up

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OBJECTIVES The purpose of this research was to study long-term left ventricular (LV) adaptations in very-high-level endurance athletes.

BACKGROUND Knowledge of cardiac changes in athletes, who are at particularly high risk of sudden cardiac death, is mandatory to detect hypertrophic cardiomyopathy (HCM) or dilated (DCM) cardiomyopathy.

METHODS We carried out echocardiographic examinations on 286 cyclists (group A) and 52 matched sedentary volunteers (group C); 148 cyclists participated in the 1995 "Tour de France" race (group A1), 138 in the 1998 race (group A2), and 37 in both (group B).

RESULTS In groups A, A1, A2, and C, respectively, diastolic left ventricular diameter (LVID) was 60.1 ± 3.9 mm, 59.2 ± 3.8 mm, 61.0 ± 3.9 mm, and 49.0 ± 4.3 mm (A vs. C and A1 vs. A2, $p < 0.0001$), and maximal wall thickness (WT) was 11.1 ± 1.3 mm, 11.6 ± 1.3 mm, 10.6 ± 1.1 mm, and 8.6 ± 1.0 mm (A vs. C and A1 vs. A2, $p < 0.0001$). Among group A, 147 (51.4%) had LVID >60 mm; 17 of them had also a below normal (<52%) left ventricular ejection fraction (LVEF). Wall thickness exceeded 13 mm in 25 athletes (8.7%) (always <15 mm), 23 with LVID >55 mm. In group B, LVID increased (58.3 ± 4.8 mm to 60.3 ± 4.2 mm, $p < 0.001$) and WT decreased (11.8 ± 1.2 mm to 10.8 ± 1.2 mm, $p < 0.001$) with time.

CONCLUSIONS Over one-half of these athletes exhibited unusual LV dilation, along with a reduced LVEF in 11.6% (17 of 147), compatible with the diagnosis of DCM. Increased WT was less common (always <15 mm) and scarce without LV dilation (<1%), eliminating the diagnosis of HCM. Serial examinations showed evidence of further LV dilation along with wall thinning. These results might have important implications for screening in athletes. (J Am Coll Cardiol 2004;44:144–9) © 2004 by the American College of Cardiology Foundation

Athlete's heart is characterized by a physiologic increase in left ventricular (LV) wall thickness (WT) and mass, together with cavity dilation in the case of endurance activities (1). Professional cyclists demonstrate the largest increase in both cavity size and WT due to a combination of extreme volume and pressure overload (2). Although such modifications are well known, reports on large homogeneous groups of highly trained athletes, who are particularly at risk of sudden cardiac death, are scarce. Furthermore, no long-term studies on LV morphology and function are available.

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However, such data might help us to detect cardiac diseases. Moreover, the performances of professional cyclists have considerably improved in recent years. In the Tour de France, the mean speed increased from 36 km/h in 1985 to 40 km/h in 1998, and the mean workload developed by the winner reached 370 W in 1991 compared with 445 W in 1995. It is also likely that many performance enhancers were used during this period (3,4). As a part of the systematic medical follow-up, which is mandatory in France, we performed echocardiographic examinations on the participants in the 1995 and 1998 Tour de France races.

METHODS

Study population. Professional cyclists (group A) participating in the 1995 (group A1) or 1998 (group A2) Tour de France or both (group B) underwent a screening echocardiogram. In 1995, 148 of the 198 participants agreed to be examined, and in 1998, 138 of the 198 agreed. All examinations were performed during the two days preceding the race by the same investigator (E.A.) using a Sonos 2500 Hewlett Packard echograph machine (Philips, Andover, Massachusetts) equipped with a 2.5-MHz probe. Thirty-seven athletes (group B) who participated in both races were examined twice. A control group of 52 young male physicians (group C) matched for body surface area (BSA) was also evaluated between September 1995 and February 1996. Part of echographic data (mean LV diameter and mass)

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Manuscript received November 18, 2003; revised manuscript received January 24, 2004, accepted February 17, 2004.

Abbreviations and Acronyms

BSA = body surface area
DCM = dilated cardiomyopathy
eFS = endocardial fractional shortening
ESS = meridional end-systolic stress
HCM = hypertrophic cardiomyopathy
LV = left ventricle/ventricular
LVEF = left ventricular ejection fraction
LVH = left ventricular hypertrophy
LVIDd = left ventricular internal diameter at end-diastole
LVIDs = left ventricular internal diameters at end-systole
mFS = midwall fractional shortening
WT = wall thickness

concerning group A1 and group C has been previously published (5).

Measurements. For each subject, at least three two-dimensional-guided M-mode recordings of the LV were recorded on videotapes. Paper tracings were obtained simultaneously. All recordings were performed as recommended by Devereux et al. (6) and by the American Society of Echocardiography (7). Readings were taken after all recordings had been completed, and LV measurements were averaged over three cardiac cycles. The parameters recorded included left ventricular internal diameters at end-diastole (LVIDd) and left ventricular internal diameters at end-systole (LVIDs), end-diastolic interventricular septal wall thickness (IVSTd), and posterior wall thickness (PWTd). All readings were taken from anonymous tracings by a single investigator (E.A.). The Devereux-modified American Society of Echocardiography-cube formula was used to calculate LV mass (6) as: 0.8 [1.04 (LVIDd + PWTd + IVSTd)^3 − LVIDd^3] + 0.6 g, which was expressed as a function of BSA (indexed left ventricular mass, g/m^2). Relative WT was calculated as (IVSTd + PWTd)/LVIDd, with a distinction between eccentric (relative WT <0.44) and concentric (relative WT ≥0.44) patterns. Left ventricular volumes were calculated using the Teichholz formulas [7/(2.4 + LVID) × LVID^3] and were used to calculate left ventricular ejection fraction (LVEF, %); cardiac output and index were derived from LVEF and heart rate. Endocardial fractional shortening (eFS) and midwall fractional shortening (mFS) were calculated as previously described (8). End-systolic meridional stress (ESS) was calculated as [(0.334 × SBP × LVIDs)/(PWTs × [1 + (PWTs/LVIDs]) (9), where SBP is the systolic blood pressure and PWTs is the systolic posterior WT.

Left ventricular hypertrophy (LVH) was defined as IVSTd and/or PWTd >13 mm and abnormal cavity dilation as LVIDd >60 mm (10,11). Thresholds corresponding to mean ± 1.96 SD of data obtained in the control group were also used to define LV dilation (LVIDd

Table 1. Main Characteristics of the Study Population

	Cyclists	Controls	p*	Cyclists 1995	Cyclists 1998	p†
n	286	52		111	101	
Age (yrs)	28.4 ± 3.2	26.3 ± 4.0	<0.0001	28.5 ± 3.4	28.1 ± 3.2	0.46
Weight (kg)	71.0 ± 6.4	71.0 ± 8.8	0.93	71.6 ± 6.6	70.2 ± 6.2	0.11
Height (cm)	179 ± 6	177 ± 6	0.07	179 ± 6	179 ± 6	0.77
BSA (m^2)	1.89 ± 0.11	1.87 ± 0.14	0.37	1.89 ± 0.12	1.88 ± 0.11	0.35
HR (beats/min)	51.8 ± 8.6	70.7 ± 13.4	<0.0001	51.7 ± 8.0	51.2 ± 9.2	0.67
LVIDd (mm)	60.1 ± 3.9	49.0 ± 4.3	<0.0001	59.4 ± 3.3	61.2 ± 3.8	0.0003
(range)	(49–73)	(41–60)		(51–68)	(49–73)	
LVIDdi (mm/m^2)	31.9 ± 2.2	26.2 ± 2.2	<0.0001	31.5 ± 2.0	32.7 ± 2.4	<0.0001
LVIDs (mm)	39.7 ± 4.1	31.4 ± 4.1	<0.0001	38.5 ± 3.2	41.6 ± 4.3	<0.0001
IVSTd (mm) (range)	11.1 ± 1.3	8.6 ± 1.0	<0.0001	11.5 ± 1.3	10.5 ± 1.0	<0.0001
	(8.7–14.8)	(7.0–10.7)		(8.7–14.8)	(8.8–13.2)	
PWTd (mm) (range)	10.0 ± 1.0	8.0 ± 0.9	<0.0001	10.2 ± 1.2	9.8 ± 0.7	0.0018
	(6.5–13.8)	(6.5–11.2)		(6.5–13.8)	(8.0–12.5)	
LVMi (g/m^2)	141 ± 21	73 ± 11	<0.0001	143 ± 22	138 ± 17	0.08
(range)	(84–222)	(50–99)		(88–192)	(84–177)	
RWT	0.354	0.342	0.06	0.37 ± 0.04	0.33 ± 0.04	<0.0001
LVEF (%) (range)	61.6 ± 6.4	65.3 ± 6.7	0.0002	63.6 ± 5.3	59.1 ± 6.8	<0.0001
	(41–77)	(52–77)		(50–75)	(41–77)	
eFS (%)	33.9 ± 4.6	36.1 ± 5.0	0.0016	35.3 ± 4.0	32.1 ± 4.8	<0.0001
mFS (%)	17.3 ± 1.9	18.5 ± 2.0	<0.0001	17.4 ± 1.9	17.2 ± 2.0	0.14
CO (l/mn)	5.7 ± 1.3	5.2 ± 1.3	0.009	5.8 ± 1.1	5.7 ± 1.5	0.73
CI (l/mn/m^2)	3.0 ± 0.7	2.7 ± 0.6	0.007	3.0 ± 0.6	3.0 ± 0.7	0.85
ESS (10^3 dynes/cm^2)	63.7 ± 15.5	58.4 ± 13.2	0.02	55.2 ± 10.9	75.0 ± 13.6	<0.0001

*Cyclists versus controls; †1995 cyclists versus 1998 cyclists.

BSA = body surface area; CI = cardiac index; CO = cardiac output; eFS = endocardial fractional shortening; ESS = meridional end-systolic stress; HR = heart rate; IVSTd = end-diastolic interventricular septal thickness; LVEF = left ventricular ejection fraction; LVIDd = left ventricular internal diameter at end-diastole; LVIDdi = indexed diastolic left ventricular internal diameter; LVIDs = left ventricular internal diameter at end-systole; LVMi = indexed left ventricular mass; mFS = midwall fractional shortening; PWTd = end-diastolic posterior wall thickness at end-systole; RWT = relative wall thickness.

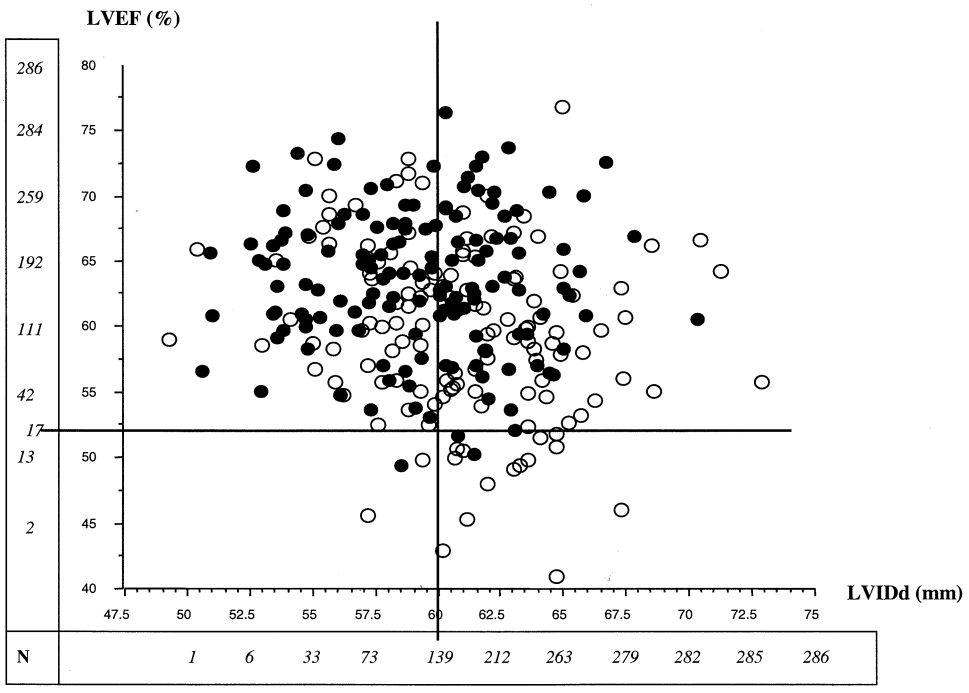

Figure 1. Plot of left ventricular ejection fraction (LVEF) against left ventricular internal diameter at end diastole (LVIDd) in all cyclists (**solid circles** = 1995; **open circles** = 1998). The **solid vertical bar** represents the normality threshold (60 mm) for LVIDd, and the **solid horizontal bar** represents the normality threshold (52%) for LVEF. Numbers in **italics** in front of each axis value are cumulative numbers of cyclists with a value below the corresponding axis value.

>57.4 mm or LVIDd >30.6 mm/m^2), low LVEF (<52%), and low mFS (<14.5%). To take into account afterload, we used the relationship between LVEF and ESS in the control group and in the athletes. Using each model, we calculated the lower limit of the 95% confidence interval of a predicted LVEF for each individual ESS (12). The difference between this last value and the measured value was used to classify subjects: athletes with difference ≤0 were considered as having abnormally low LVEF.

Statistical analysis. Statistical analysis was performed with the StatView software (Version 4.5, SAS, Inc., Cary, North Carolina). Results are presented as means ± 1 SD. Differences between two groups were compared by an unpaired *t* test, and differences between more than two groups were tested by one-way analysis of variance. The paired *t* test was used to assess change within a group. For paired comparisons, the Bonferroni correction was used to take into account multiple comparisons. Differences were considered to be statistically significant if $p < 0.05$.

RESULTS

The main characteristics of the study groups are presented in Table 1. There were no differences in height, weight, and BSA between the 286 athletes and the 52 control subjects. Systolic blood pressure (120 ± 9 mm Hg vs. 126 ± 13 mm Hg, $p < 0.0001$) and diastolic blood pressure (68 ± 9 mm Hg vs. 77 ± 10 mm Hg, $p < 0.0001$) were lower in athletes than in controls, as was heart rate.

LV morphology. Wall thickness and cavity dimensions were greater in athletes than in controls (Table 1); LVIDd was correlated with BSA ($r = 0.37$, $p < 0.0001$) but not with age ($r = 0.002$, $p = 0.98$) or heart rate ($r = -0.015$, $p = 0.80$). Left ventricular internal diameter at end diastole exceeded the upper limit of normal (57.4 mm) in 214 athletes (75%), with values above 60 mm in 147 cases (51% vs. 0% in controls) and above 70 mm in four cases (Fig. 1). Maximal WT exceeded 13 mm in 25 cyclists (8.7% vs. 0% in controls, always <15 mm), 23 of whom had an LVIDd >55 mm (Fig. 2). The LV geometry was eccentric in 273 athletes and concentric in 13. In all athletes but one, LV morphology was symmetrical (relative WT <1.5), although 20 athletes had a relative WT >1.3.

LV function. The LVEF was ≤60% in 111 athletes, between 40% and 52% in 20 athletes, and between 52% and 56% in 38 athletes (Fig. 1). Although cardiac output and cardiac index were higher in athletes than in controls, indexes of endocardial and midwall LV function (LVEF, eFS, mFS) were all significantly lower in athletes (Table 1). Moreover, LVEF was lower in the 147 cyclists with LV dilation (>60 mm) than in the remaining 139 cyclists (60.5 ± 6.9% vs. 62.8 ± 5.6%, $p = 0.0027$). Conversely, among the cyclists with abnormal LV dilation, 67 of 147 (46%) had an LVEF <60%, vs. 39 of 139 (28%) of those with normal LV size ($p = 0.0021$). The mFS was abnormally low in 26 cyclists (22 with eccentric LVH) who showed lower LVEF (51.5 ± 4.9% vs. 62.6 ± 5.6% for the remaining 260 athletes, $p < 0.0001$). Finally, 17 athletes (14 in 1998, 3 in

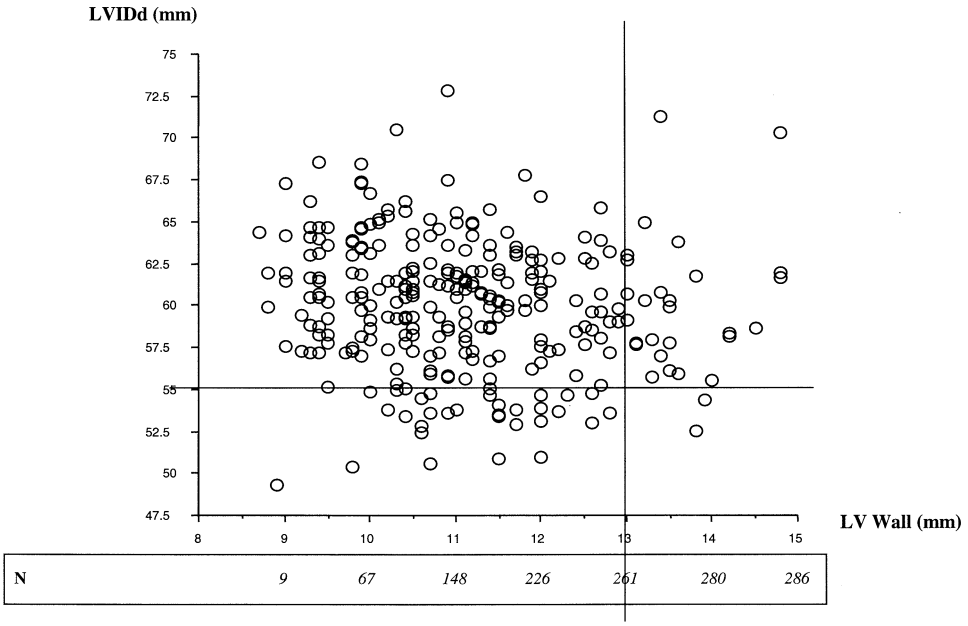

Figure 2. Plot of left ventricular internal diameter at end diastole (LVIDd) against maximal wall thickness (WT) in all cyclists. The **solid horizontal bar** represents the LVIDd threshold for dilated left ventricle (LV) (55 mm), and the **solid vertical bar** represents the normality threshold for maximal WT (13 mm). Numbers in **italics** in front of the X axis values are cumulative numbers of cyclists with a value below the corresponding axis value.

1995) showed both LV dilation (>60 mm) and low LVEF (<52%) (Fig. 1). Ten of these athletes had also a low mFS (<14.5%). Comparisons between measured LVEF and predicted LVEF (lower limit of the 95% confidence interval) are shown in Figure 3. All the controls are above the zero line: measured LVEF values are always higher than predicted LVEF values. In the subgroup of 17 cyclists with both LVIDd >60 mm and LVEF <52%, 7 cyclists are below or at the zero line, which means that they might be classified as abnormal. Moreover, three cyclists with LVEF <52% and an LVIDd between 58 mm and 60 mm also have lower than predicted LVEF values.

Comparison between 1995 and 1998. Cyclists who took part in the 1998 race had a larger LV cavity and thinner walls than those who participated in the 1995 race (Table 1). Thus, those who raced in 1998 had a more eccentric LV geometry. In 1995, one cyclist had an LVIDd >70 mm compared with three cyclists in 1998 (one cyclist

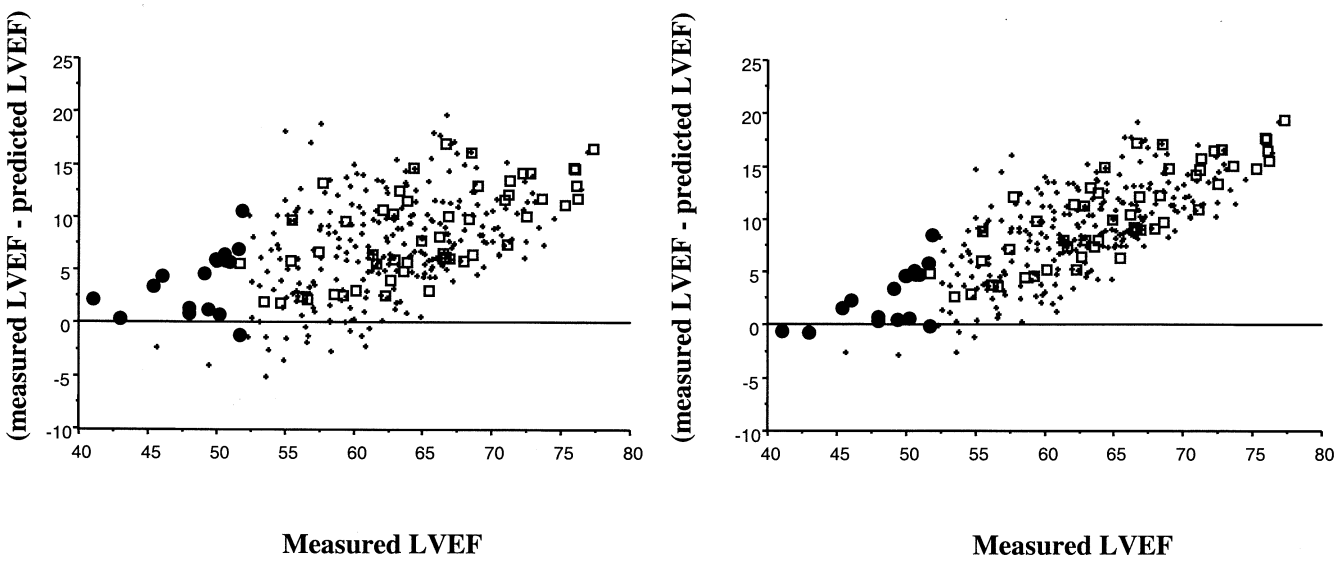

Figure 3. Plot between the measured left ventricular ejection fraction (LVEF) (X axis) and the difference between measured LVEF and the lower limit of the 95% confidence interval of the predicted LVEF for a given end systolic stress (ESS) (Y axis). **(Left)** Predicted LVEF was defined by the model obtained in controls (LVEF = 87.55 − 0.38 · ESS, r = 0.75, $p < 0.0001$). **(Right)** Predicted LVEF was defined by the model obtained in cyclists (LVEF = 80.34 − 0.29 · ESS, r = 0.71, $p < 0.0001$). Results are shown for the 17 cyclists with both left ventricular internal diameter at end diastole >60 mm and LVEF <52% **(solid circles)**, the remaining cyclists (n = 269) **(+)**, and the control group (n = 52) **(open squares)**.

Table 2. Echocardiographic Characteristics of the Subgroup of 37 Cyclists That Participated in Both the 1995 and 1998 Races

	1995	1998	p Value
LVIDd (mm)	58.3 ± 4.8	60.3 ± 4.2	0.001
BSA (m^2)	1.89 ± 0.11	1.89 ± 0.11	0.16
LVIDdi (mm/m^2)	30.9 ± 2.4	32.0 ± 1.8	0.0011
LVIDs (mm)	37.8 ± 4.2	40.3 ± 3.9	<0.0001
IVSTd (mm)	11.8 ± 1.2	10.8 ± 1.2	0.0002
PWTd (mm)	10.6 ± 1.0	9.9 ± 0.8	0.0014
LVMi (g/m^2)	144 ± 23	138 ± 21	0.05
RWT	0.39 ± 0.05	0.35 ± 0.03	<0.0001
LVEF (%)	63.5 ± 6.3	60.8 ± 5.7	0.01
eFS	35.2 ± 4.7	33.3 ± 4.1	0.019
mFS	17.0 ± 2.0	17.4 ± 1.9	0.32

Abbreviations as in Table 1.

took part in both races). A similar pattern was observed in athletes who participated in both races (group B) (Table 2).

DISCUSSION

Echocardiographic screening is mandatory in highly trained athletes to detect a dilated (DCM) or hypertrophic (HCM) cardiomyopathy. In our study, based on a large and homogeneous cohort of professional bicyclists participating in the Tour de France races in 1995 and 1998, most athletes (51%) displayed a substantial LV enlargement, 11.6% with indexes of depressed myocardial performance. Moreover, unexpected changes in echocardiographic LV morphology were observed between the two races.

LV structure evaluation. Endurance cycling has the greatest impact on LV cavity dimension and WT, due to a combination of endurance training (cycling) and isometric exercise (with the arms). Thus, while LV enlargement exceeding 60 mm (13) is unusual in non-elite athletes, this is observed in about 14% of elite athletes (11). We report here the largest proportion ever published of athletes with substantial LV enlargement (51% >60 mm, up to 73 mm). The major determinants of dilation are usually BSA, as is the case here, and participation in "high-impact" sports such as cycling, cross-country skiing, canoeing, rowing, and soccer. However, unlike in a previous study (11), considerable LV dilation persisted here after correction for BSA. Even in the group of 62 athletes with BSA <1.8 m^2, 22 (35%) exhibited abnormal LV dilation (Table 3). Increased LV WT was less common (9% of the athletes) and similar to that previously reported (14). It never exceeded 15 mm and rarely occurred in the absence of cavity dilation (<1%), allowing easy elimination of the diagnosis of HCM (Fig. 2) (15).

Abnormal systolic performance. Although global LV systolic function was within the normal range for the whole population, half of the cyclists with abnormal dilation had LVEF below 60%, and 17 of the 21 athletes with an abnormally low LVEF (≤52%) showed an increased LV size (>60 mm). In a previous study (11), athletes with LV dilation showed a normal global systolic function. Moreover, in a small group of 21 less trained elite cyclists (16), as demonstrated by a lower mean LV mass (200 g vs. 266 g in our study), LVH was not associated with significant abnormalities of cardiac function. It has been suggested that reduced fractional shortening in runners (who show predominant LV dilation) could be due to a decreased preload along with a normal afterload and contractile state (17). It has also been shown that 39% of football players have a moderately reduced resting LVEF (50% to 55%), which appropriately increases with exercise (mean, 76%) (18). In the present study, whatever the approach used to define abnormal LV function (association of LV dilation and low LVEF or low afterload-corrected LVEF) (Fig. 3), a depressed myocardial function can be suggested in a small group of cyclists (17). It is unlikely that these subjects had a pre-existing DCM, as this condition is very scarce in the general population (<36 of 100,000) (19,20). The potential role of exercise-induced tachycardia can be excluded, as all cyclists carefully monitored their heart rate during training and the races, with a similar average exercise heart rate (around 80% of their maximal heart rate to avoid muscular exhaustion). It is also possible that illicit drugs might induce LV function deterioration. This factor has not yet been studied in detail, even though there is evidence that some drugs are becoming more popular among athletes (3). Recent works do not mention potential drug abuse (2), or eliminated this possibility on the questionable basis that athletes denied the use of illicit drugs (11,21). Moreover, the combined effects of multiple drugs remain unknown.

Table 3. Comparison of LVIDd in a Subset of Athletes Engaged in High Impact Sports (Cycling, Cross-Country Skiing, Canoeing, Rowing, and Soccer) (10) and in Professional Cyclists (Current Study) According to BSA

BSA	Pellicia et al. (10)	Current Study
≤1.8 m^2	54.6 ± 3.5	58.1 ± 3.9
	n = 52	n = 62
1.81–2 m^2	56.3 ± 3.6	60.1 ± 3.6
	n = 179	n = 178
>2 m^2	59.0 ± 3.2	62.6 ± 3.6
	n = 86	n = 46

BSA = body surface area; LVIDd = left ventricular internal diameter at end-diastole.

Serial cardiac changes. Successive examinations in 1995 and 1998 in the subgroup of 37 cyclists evaluated twice showed further LV dilation along with wall thinning with time. This was not associated with a decrease in cyclist performances (Indurain won the 1995 Tour de France—3,635 km—at a mean speed of 39 km/h, whereas Pantani won the 1998 Tour de France—3,711 km—at a mean speed of 40 km/h). In 1998, LV diameters were markedly increased, with the largest dimension ever reported in athletes (73 mm). The 2-mm difference in diameter observed between 1995 and 1998 in this cohort is of the magnitude observed between athletes practicing isotonic and isometric sports (2). It seems unlikely that this difference was due to poor reproducibility of these anonymous readings. In a

previous study involving 96 cyclists, the mean interobserver or intraobserver difference for LV diameters was ≤0.3 mm (22). A second bias could be due to seasonal changes in LV morphology: WT is lower during the resting season than during the competitive season, whereas diameters remain unchanged (23). In our study, all measurements were taken at the same moment in the competitive season in 1995 and 1998. Moreover, the difference observed in the group of cyclists examined twice was similar to that observed in the whole population, eliminating the possibility that the extremely large LV cavities found in certain athletes are due to a specific genetic background (24). Finally, it has been suggested that heart rate affects M-mode echocardiographic LV measurements (25). However, in our study, heart rate was not significantly different between the two evaluations. In the absence of such bias, LV changes may be due to changes in the type and intensity of physical training. However, to induce a 2-mm difference in LV diameter at the same moment of the season, training technology must change dramatically, and no such change has been reported. Moreover, more intensive and/or prolonged physical training would have lead to wall thickening (23,26), which was not observed in our population. The unexpected and significant decrease in WT observed with time might also be due to the increasing problem of drug abuse.

Conclusions. In this large homogeneous cohort of highly trained elite cyclists, marked echocardiographic LV dilation is frequent and often associated with a low LVEF, which raises the problem of the differential diagnosis with a dilated cardiomyopathy. Abnormal increases in WT were less common, always moderate, and usually associated with cavity dilation, eliminating a primary pathologic hypertrophy. The unexpected occurrence of cavity dilation and wall thinning with time raises questions about excessive physical training and/or pharmacologic interventions. These results might have important implications for myocardial disease screening in highly trained elite athletes.

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