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FASTTRACK CLINICAL RESEARCH

Mortality of French participants in the Tour de France (1947–2012)

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Aims In the context of recent concerns regarding performance enhancing techniques and potential negative health effects of high-level physical activity, data on the long-term outcomes and causes of death in elite endurance cyclists are of particular interest.

Methods and results Characteristics and vital status of all French participants in the Tour de France were collected for the 1947–2012 period. Causes of death were obtained from 1968. Overall and disease-specific mortalities were compared with the French male population using overall and specific standardized mortality ratios (SMRs) with their 95% confidence intervals (CIs). Among the 786 French cyclists who participated at least once between 1947 and 2012, 208 (26%) died by 1 September 2012. Neoplasms and cardiovascular diseases accounted for 61% of deaths. We observed a 41% lower mortality in French cyclists (SMR: 0.59, 95% CI: 0.51–0.68, $P < 0.0001$), which did not change over time ($P = 0.70$). It was observed for main mortality causes: for neoplasms (SMR: 0.56; 95% CI: 0.42–0.72, $P < 0.0001$) and for cardiovascular death (SMR: 0.67; 95% CI: 0.50–0.88, $P = 0.004$), except mortality related to external causes (SMR: 1.06, 95% CI: 0.71–1.53, $P = 0.80$).

Conclusion We observed a substantially and significantly lower mortality in participants in the Tour de France, compared with the general male population. However, our results do not allow us to assess in detail the balance between positive effects of high-level sports activity and selection of healthy elite athletes, vs. any potential deleterious effects of excessive physical exercise or alleged doping.

Keywords Cycling • Doping • Cardiovascular • Mortality • Athletes

Introduction

The Tour de France is the world's most celebrated endurance cycling event and celebrates its 100th race in 2013.[1] The race has been held annually since 1903 except during the two World Wars. As the Tour gained prominence and popularity, the race was lengthened and its popularity extended around the globe. This is a 21 days competition with 2 days of rest during July covering more than 3200 km.

The benefit of regular physical activity is well known and has been recommended for both primary and secondary prevention of cardiovascular diseases.[2–4] While the benefit of moderate regular physical activity has been clearly demonstrated, recent controversy exists regarding the potential adverse effects of regular strenuous physical exercise.[5–7] In this context, the long-term outcome of elite athletes is of particular interest, although data are scarce on this issue.[8,9] To the best of our knowledge, there are, very few data on cycling,[10,11] and none addressed the issue of specific causes of death. The Tour de

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France is arguably one of the most physiologically demanding sports competition.[12] The effort involved has been compared with 'running a marathon several days a week for nearly three weeks', while the total elevation of the climbs was compared with 'climbing three Everests'.[13,14] In addition, as recently emphasized, the Tour de France has been the subject of many controversies because of exposure to performance enhancing techniques, in the past and still recently.[11,15] described as potentially promoting an increase in mortality.[16]

We therefore undertook a study aiming to evaluate and compare overall mortality and specific causes of death among French participants in the Tour de France from 1947 to 2012, vs. the community average.

Methods

Data collection

Data on Tour de France French participants, for the 1947–2012 period, were collected from the two official Websites (http://www.memoire-du-cyclisme.eu, http://www.letour.fr) and complemented with two other sources (http://www.wikipedia.org/, http://www.siteducyclisme.net/). Identity information was confirmed via the National Registry for Identification of Physical Persons (RNIPP) from the National Institute of Statistics Economical Studies (INSEE). The study was approved by the ethical committee Advisory Committee on Information Processing in Research in the Field of Health (CCTIRS) and the French National Commission for Data Protection and Liberties (CNIL) in 2012.

Vital status was confirmed via the National Registry for Identification of Physical Persons (RNIPP) from the National Institute of Statistics Economical Studies (INSEE). Causes of death were obtained from the French Center on Medical Causes of Death (CépiDc–INSERM), which is able to provide the causes of death occurring in France since 1968. A 2-year lag exists between the availability of mortality status and the corresponding cause of death. Therefore, in the current study, the mortality status of all the French cyclists who had participated at least once in Tour de France from 1947 to 2012 was available by September 2012, while the specific causes of deaths could be retrieved until 2010. Causes of deaths were classified according to the International Classification of Diseases (8th revision before 1978, 9th revision between 1979 and 1999, 10th Revision after 2000).

Statistical analysis

Characteristics of subjects were described as means ± SD, proportions (%), median, and inter-quartile ranges (IQR) when appropriate. The overall mortality (from 1947 to 2012) and specific causes of death (from 1968 to 2010) of the French cyclists who had participated at least once in Tour de France from 1947 to 2012 were compared with that of the French male population of comparable age during the same period. The follow-up for each cyclist was defined by the difference between the date of endpoint (1 September 2012 if alive or date of death) and the date of its first participation to the Tour de France. Person-years and standardized mortality ratio (SMR) were computed.[17] Standardized mortality ratios were calculated by 5-year-age class and 1-year interval, and their 95% confidence intervals were calculated using the exact method.[18] Standardized mortality ratio is the ratio of the number of observed deaths in our cyclists over the expected number of deaths in the cyclists if they had had the mortality rate of a referent population of similar age, here the male French population. An SMR <1 indicates lower mortality, whereas an SMR >1 indicates higher mortality in the cyclists when compared with the referent population. The period effect was explored using two complementary approaches. First, to address (indirectly) the possible effect of doping on long-term mortality, cyclists were grouped according to three 20-year-time periods of participation to the Tour de France (1947–70, 1971–90, and 1991–2010), corresponding schematically with the reported or suspected use of amphetamines, steroid, and erythropoietin, respectively.[19] Thereafter, SMRs according to the period of participation were calculated accordingly. Since only the youngest are considered for the last period, no death was observed in this group by 1 September 2012. Secondly, to account for mortality trends over time, deaths that occurred within each 20-year-time period were considered and the corresponding SMRs estimated. To further take into account a possible age period interaction, we performed a binomial model (SAS PROC GENMOD).

In addition, as an exploratory analysis, we estimated the number of additional years gained among the cyclists when compared to the general male population. For that purpose, we assessed the life span in the deceased cyclists and compared it to the life expectancy of the male general population of same age and period. This was done only in years where the deceased cyclists accounted for more than 60% of the cohort (i.e. 1947 to 1951).

Overall mortality rate from the community was calculated using the Human Mortality Database (http://www.mortality.org/). *P*-values of <0.05 were considered to indicate statistical significance. All data were analysed using SAS software v9.3 (SAS Institute, Inc., Cary, NC, USA).

Results

General population and cyclists overall mortality

A total of 786 French elite cyclists participated at least once in the Tour de France between 1947 and 2012 (*Figure 1*). With a mean participation of 2.5 Tour de France by cyclist, they represented 29.7% of the total participants. The median age at the first participation was 25.1 (23.7–26.6) years, and year of birth of the participants ranged from 1910 to 1989. The median duration (IQR) of follow-up was 37.4 (23.5–49.8) years.

Among this cohort of 786 French cyclists, 208 (26%) were known to have died by 1 September 2012. Compared with the general population, we observed a 41% lower mortality in French cyclists (SMR: 0.59; 95% CI: 0.51–0.68, $P < 0.0001$). Standardized mortality ratios were consistent across age, except for ages <30 years in whom a non-significant SMR of 1.65 (0.75–3.25) was observed (*Figure 2*). Standardized mortality ratios were also consistent after grouping cyclists by their period of participation to the Tour de France. Of the 391, 220, and 175 cyclists who participated to the Tour de France in the 1947–70, 1971–90, and 1991–2012 periods, respectively, 188, 20, and 0 had died by September 2012. This yielded SMRs of 0.59 (0.51–0.69) and 0.68 (0.39–1.11) for those who participated in the 1947–70 and 1971–90 periods, respectively. Furthermore, *Figure 3* illustrates the lower mortality in the cyclists when compared with the male general population across the three time periods (1947–70, 1971–90, and 1991–2010): 0.56 (95% CI: 0.28–1.01), 0.54 (95% CI: 0.39–0.72), and 0.62 (95% CI: 0.52–0.73), respectively (*P* for difference = 0.70, *P* for age period interaction = 0.49).

Causes of death

Although there was no loss to follow-up for total mortality, specific causes of deaths were missing in seven cyclists (three were due to death which occurred outside France and four were of

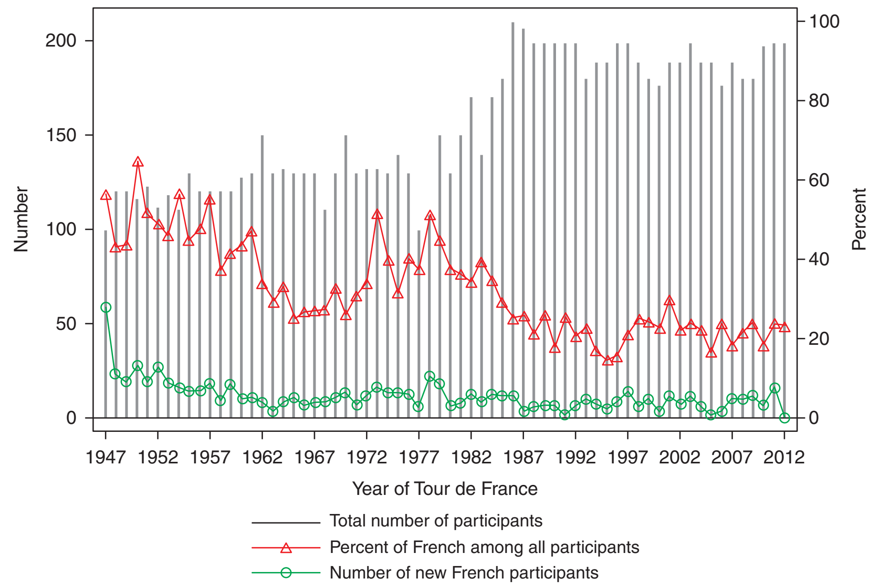

Figure 1 Proportion of French participants to the tour from 1947 to 2012.

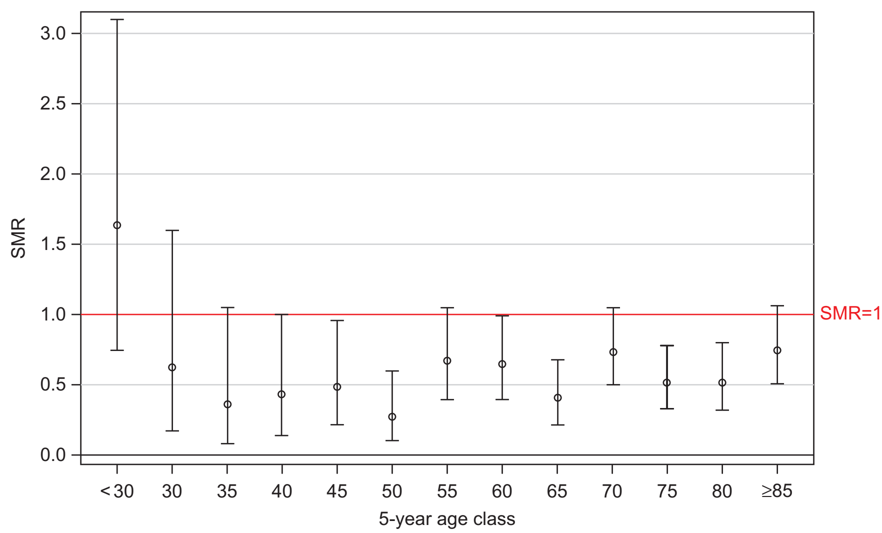

Figure 2 Standardized mortality ratio by 5-year-age class. Standardized mortality ratios were consistent across age, except for ages <30 years among whom only nine cyclists died. For this latter, an excess of mortality was suggested although the standardized mortality ratio was not statistically significant.

undetermined cause). The three principal causes of death were neoplasms (32.2%), cardiovascular diseases (29.0%), and external (mainly trauma-related) causes (15.8%). The three main cancers were digestive (35%), lung (22%), and prostate (7%). Among the 53 deaths related to cardiovascular diseases, we denoted 39 cardiac deaths (74%). Other causes of death included infectious diseases (2.2%), endocrine and nutritional diseases (2.2%), neurological (2.2%), digestive system diseases (2.2%), and genitourinary disease (1.1%). There was no death due to blood disease. Among the nine deceased cyclists aged <30 years, six (66%) were related to accidents (races and traffic accident), two to cardiac causes, and one to an unknown cause. Of note, no death occurred during the Tour de France among these 786 French participants.

Table 1 shows the SMRs for specific cause of death. Overall, the direction and the magnitude of the SMRs by cause of death were comparable to the overall SMR: neoplasms (SMR: 0.56, 95% CI:

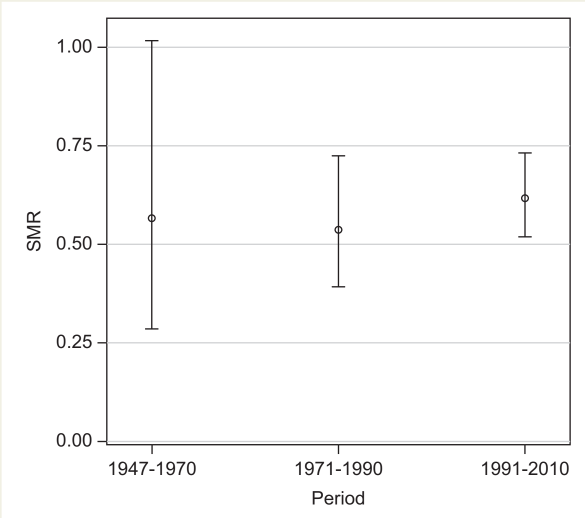

Figure 3 Standardized mortality ratio over time. We observed a lower mortality in the cyclists as compared to the male general population across the three time periods (1947–70, 1971–90, and 1991–2010), without any significant difference over time.

Table 1 Standardized mortality ratio by causes of death

	Expected Death	Observed Death	SMR	95% CI
Infectious diseases	5.44	4	0.74	(0.20–1.88)
Neoplasms	106.01	59	0.56	(0.42–0.72)
Endocrine and nutritional diseases	6.90	4	0.58	(0.16–1.48)
Mental disorders	6.61	3	0.45	(0.09–1.33)
Nervous system diseases	9.05	4	0.44	(0.12–1.13)
Cardiovascular diseases	78.87	53	0.67	(0.50–0.88)
Respiratory system diseases	17.87	5	0.28	(0.09–0.65)
Digestive system diseases	18.21	4	0.22	(0.06–0.56)
Musculoskeletal diseases	1.11	1	0.90	(0.02–5.02)
Genitourinary system diseases	3.66	2	0.55	(0.07–1.98)
Ill-defined conditions	14.03	8	0.57	(0.25–1.12)
External causes	27.29	29	1.06	(0.71–1.53)

Causes of deaths were classified according to the International Classification of Diseases (8th revision before 1978, 9th revision between 1979 and 1999, 10th Revision after 2000).

0.42–0.72, $P < 0.0001$), cardiovascular diseases (SMR: 0.67, 95% CI: 0.50–0.88, $P = 0.004$), and respiratory system diseases (SMR: 0.28, 95% CI: 0.09–0.65, $P = 0.003$), digestive system diseases (SMR: 0.22, 95% CI: 0.06–0.56, $P = 0.001$). However, no clear difference was observed between cyclists and the general population regarding mortality related to external causes (SMR: 1.06, 95% CI: 0.71–1.53, $P = 0.80$).

To put into perspective the potential benefit in terms of life-years gained, we estimated the additional life span of cyclists who participated to the Tour. Among the 109 cyclists who participated in the Tour between 1947 and 1951, mean additional life span was 6.3 years compared to the general population.

Discussion

We observed a significant 41% lower mortality among French elite cyclists from the Tour de France, compared with the general male population. This reduction in overall mortality was relatively homogeneous across ages (except for ages <30), time periods, and major causes of death (except for external causes of death).

It has been traditionally suggested that a higher dose of physical activity has an additional benefit on reducing all-cause mortality (that is, a dose–response relationship).[20,21] The recent results of two large cohort studies have proposed the concept of a U curve, with a strong benefit of moderate physical activity, but possibly a deleterious effect in case of particularly strenuous and sustained physical activity.[5,6] These new findings have been illustrated by recent basic and clinical published data on the effects of 'excessive' sport exposure and cardiac remodelling.[7,22–27] Training induces volume- and time-dependent morphological and functional changes in the heart. Heart rhythm disorders, such as atrial arrhythmia (including atrial fibrillation and atrial flutter), are a well-established association with such long-term endurance practice.[28,29] Veteran athletes have a higher prevalence of atrial fibrillation and sinus node disease.[28–30] It has been also recently suggested that long-term excessive exercise may accelerate ageing in the heart, as evidenced by increased coronary artery calcification, diastolic ventricular dysfunction and large-artery wall stiffening.[31] Finally, although shorter exercise duration has been associated with favourable antioxidant and vascular effects, longer exercise seems to blunt these beneficial effects and to yield adverse effects on vascular function.[32]

The observed significant reduction in overall mortality in our cohort of French participants in the Tour de France, compared with the community average, should be interpreted with caution for the following reasons. First, there is a significant selection bias, as only the healthiest and fittest individuals are likely to be able to compete at such elite levels.[33] Such excellence in sport may be due in part to genetic predisposing factors.[9,34,35] On the other hand, the reference population includes males from the community with potentially prevalent chronic disease and illness putting them at a higher risk of death, exaggerating, therefore, the difference in mortality between the cyclists of the Tour de France and the community average. Secondly, participation in the Tour de France and the preceding years of training represent a relatively small part of each athlete's lifespan, and thus it is hard to attribute the observed lower mortality solely to participation in the Tour de France. Thirdly, and as a corollary, confounding factors may have played a role in this observed lower mortality. In particular, data on the lifestyle habits after their athletic career would have been informative but were unfortunately unavailable in the present study. Interestingly, former elite athletes, especially endurance athletes, tend to maintain active and healthy lifestyles later in life, by engaging in more physical activity and smoking less than those in the general population.[36–38]

As recently emphasized, the Tour de France seems to have been the matter of controversies because of exposure to performance enhancing techniques.[14] Doping is associated with serious health complications, of which the most common and especially dangerous involve the cardiovascular system.[18] Doping may have attenuated the association between participation to the tour de France and lower long-term mortality in our cohort. Three main periods of prohibited substances use have been described: amphetamines and cocaine use in the 1950–60s; androgens and anabolic steroids use between the 1970s and 80s, and since 1990, the use of growth hormone and erythropoietin. Although we could not directly estimate the effect of doping, analysis by time period is rather reassuring. These are exploratory analysis and we lacked time of follow-up for the last period, i.e. the possible effect of erythropoietin on long-term mortality.

To the best of our knowledge, comparable data on overall mortality among elite cyclists are only available from the study of Sanchis-Gomar *et al.*[10] Although their data have added substantial information to the field, their findings remained limited to cyclists who participated to the Tour de France before 1964, without specific cause of death analysis. Specific cause of death analysis has been addressed in athletes in general or in specific sports such as soccer, American football, and cross-country skiing.[8,39–43] Our findings confirm the significant reduction in overall mortality, as well as the relatively homogeneous risk reduction distributed across different causes of death. Notably, we found particularly low-specific mortality rates regarding cancer and cardiovascular diseases compared with the general population of the same age. In contrast, we did not observe any excess mortality in any specific mode of death, contrasting, for example, with the experience among American Football league players (with neurodegenerative mortality estimated to be three times higher than that of the general US population, possibly related to the higher chronic traumatic encephalopathy), or among soccer players (who had more amyotrophic lateral sclerosis) reported so far. However, these studies are limited by the relatively few absolute numbers of deaths, as well as large differences in the accuracy of death certificates in different areas of the same country.[39,40,44] Furthermore, we found consistent lower mortality across age group. Notably, a non-significant excess mortality was observed in the youngest. Although speculative, these young cyclists may harbour cardiomyopathy or ion channel disease that is more likely to trigger a sudden death during such demanding effort.[45–48] In our study however, a particularly high frequency of death related to traffic or race accident was observed in that young age group.

Although we report here the first cause of death analysis among elite cyclists compared with the general French population and had no loss of follow-up regarding their mortality status, we acknowledge some limitations. First, as an observational study, no causal inference can be made between participation in the Tour and the observed lower mortality. In particular, except age, and time periods, we were not able to adjust for potential confounding factors. Secondly, French cyclists represent only 30% of all Tour participants, and the extent to which these results apply to other nationalities is uncertain.[11] Although genetic background and some environmental factors may differ between countries, it seems likely that the characteristics of such highly selected athletes are broadly comparable across countries. Third, analysis was restricted to mortality while morbidity and quality of life data were not available. Finally, the reliability of death certificates for the diagnosis of the causes of death and of sudden death in particular is questionable.[49]

Conclusion

We observed a substantially and significantly lower mortality in participants in the Tour de France, compared to the general male population. However, our results do not allow us to assess in detail the balance between positive effects of high level sports activity and selection of healthy elite athletes, vs. any potential deleterious effects of excessive physical exercise or alleged doping.

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Conflict of interest: none declared.

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