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Letter to editor

Cardiac Biomarkers and Cycling Race

Dear Editor-in-chief,

In cycling as in other types of strenuous exercise, there exists a risk of sudden death. It is important both to understand its causes and to see if the behavior of certain biomarkers might highlight athletes at risk. Many reports describe changes in biomarkers after strenuous exercise (Nie et al., 2011), but interpreting these changes, and notably distinguishing normal physiological responses from pathological changes, is not easy. Here we have focused on the kinetics of different cardiac biomarkers: creatin kinase (CK), creating kinase midbrain (CK-MB), myoglobin (MYO), highly sensitive troponin T (hs-TnT) and N-terminal brain natriuretic peptide (NT-proBNP). The population studied was a group of young trained cyclists participating in a 177-km cycling race. The group of individuals was selected for maximal homogeneity. Their annual training volume was between 10,000 and 16,000 kilometers. The rhythm of races is comparable and averages 35 km/h, depending on the race's difficulty.

The cardiac frequency was recorded via a heart rate monitor. Three blood tests were taken. The first blood test, T_0, was taken approximately 2 hours before the start of the race and was intended to gather values which would act as references for the following tests. The second blood test, T_1, was realized within 5 minutes of their arrival. The third and final blood test, T_3, was taken 3 hours following their arrival. The CK, CK-MB, MYO, hs-TnT and NT-proBNP were measured on the Roche Diagnostic modular E (Manhein, Germany). For the statistical analysis, an ANOVA and post hoc test of Scheffé were calculated with the Statistica Software version 9.1.

We noticed an important significant variation in the cardiac frequency between T0 and T1 ($p < 0.0001$), T0 and T3 ($p < 0.0001$), and T1 and T3 ($p < 0.01$). Table 1 shows the results obtained for the different biomarkers. CK and CK-MB showed significant variation between T0-T1 and T0-T3 ($p < 0.0001$). Myoglobin increased significantly between T0 and T1 ($p < 0.0001$), before decreasing between T1 and T3 with the T3 levels remaining higher than T0 ($p = 0.01$). The changes in myoglobin and CK observed here probably reflect skeletal muscle damage rather than injury to cardiomyocytes (Le Goff et al., 2012). During a Marathon, it has been clearly observed a post-effort increase of CK-MB and myoglobin, accompanied by an increase in hs-TnI release, without demonstrating any presence of micro-infarction by myocardial scintigraphy (Shave et al., 2012).

HsTnT increased significantly between T0 and T1 ($p < 0.0001$) and stayed high 3 hours after the end of the exercise (T0-T3: $p < 0.0001$).

At T0, the values obtained for NT-proBNP were inside the normal range, but we noted an increase with time. Some subjects were above the upper reference value at T1. The intense exercise produced during the race induced a significant increase of NT-proBNP (Tschope et al., 2005). This evolution is probably due to increased parietal pressure, as a rise in NT-proBNP can be a physiological response to increased ventricular pressure at the end of the diastole (Scharhag et al., 2008). They had no particular physical complaints during or after the exercise, this marker is useful for the detection of diastolic dysfunction in patients with exertion dyspnea. We observed the same kinetic as for hs-TnT. We noticed statistically significant variation between T0 and T1 ($p < 0.01$) and stayed high 3 hours after the end of the exercise (T0-T3: $p < 0.0001$). At the start of the race, three of our cyclists showed levels of hs-TnT below the reference level. At the end of the race, all of them showed a rise above the cut-off, however, probably not indicative of any permanent damage to the heart. It is worth noting that the cyclists with the highest pre-race levels showed only a moderate post-race increase.

Since two cyclists (4 and 6 in Table 1) had levels of hsTnT above 100 ng/L at T1, a cut-off used in diagnosis of acute myocardial infarction. According to these

Table 1. Results for the cardiac biomarkers analyzed (with their correspondent reference range) at the 3 different times.

	CK (30-175 U/L)			CK-MB (0-6 µg/L)			Myo (28-72 µg/L)			hsTnT (<14 ng/L)			NT-proBNP(5-103 ng/L)		
Subjects	**T0**	**T1**	**T3**	**T0**	**T1**	**T3**	**T0**	**T1**	**T3**	**T0**	**T1**	**T3**	**T0**	**T1**	**T3**
1	119	223	223	5,8	11,1	12,0	25	110	73	5	43	48	25	69	66
2	95	188	185	4,6	9,0	9,5	30	109	64	5	58	40	14	32	30
3	155	237	262	3,4	6,0	7,0	22	106	92	5	49	47	73	203	188
4	295	320	356	6,9	7,4	9,0	22	94	68	8	105	79	20	39	44
5	116	151	216	3,4	4,0	5,7	28	94	98	6	33	26	26	57	67
6	260	326	340	6,2	7,3	7,7	30	203	104	7	108	88	16	45	35
7	121	145	147	3,2	3,6	3,9	25	49	37	5	13	14	16	39	36
8	177	203	196	7,8	4,6	4,9	32	85	60	18	36	35	55	225	161
9	174	212	240	4,4	7,7	9,0	47	144	110	17	33	37	140	82	67
10	142	194	189	2,7	3,5	4,0	25	59	48	5	33	49	13	27	22
11	90	127	159	2,0	2,7	3,6	24	79	61	5	33	42	51	86	82
12	218	255	227	4,9	5,6	5,8	38	121	120	5	18	17	49	83	68
13	113	129	134	5,0	5,3	5,4	31	48	53	15	27	34	38	64	55
14	316	338	323	4,6	4,9	5,0	38	102	71	5	16	13	35	78	54

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results we could think that we have too a notion of high and low responders as with the CK, well described in the work of Hody et al. (2013).

Also interesting is the fact that both subjects showing the highest hsTnT levels at T1 had unexceptional NT-proBNP levels, and the two individuals having the highest NT-proBNP levels had unexceptional hsTnT values. These two markers would appear to give independent types of information on the effect of exercise on the heart. Due to the various mechanisms in cause, the impact on NT-proBNP and TnT is not the same. It should thus necessary to characterize the response of the left ventricle, the right ventricle and auricles to explain these different responses. To interpret these values, it is too necessary to remember that the intra-individual biological variations can go up to 70% for NT-proBNP and 30% for TnT (Vasile et al, 2010). However, as variations of 100% for TnT and from 11 to 200% for NT-pro-BNP were observed, these observations could be really due to the effort and not due only to intra-individual biological variations. Moreover, both of these markers are eliminated via the kidneys, but of course the serum level reflects a balance between release and degradation. One of the high-NT-proBNP cyclists had fairly high levels of renal markers, but the other did not.

Perhaps our most interesting results concern cyclist number 6 (Table 1): this cyclist showed high values of CK and the highest levels of hsTnT and myoglobin. As myoglobinemia can be indicative of renal impairment (Neumayr et al., 2005) and as cTnT is degraded and then eliminated via the kidneys, this points to a particularly strong impact of exercise on renal function in this individual. Regarding hsTnT, however, it should be noted that the other cyclists showing an unusually high level of this biomarker had reasonable levels of myoglobinemia.

In conclusion, concentrating on the most extreme observed rises in cardiospecific biomarkers (probably not indicative of any permanent damage to the heart), we note that the individuals showing the highest hs-TNT levels are not the same as those showing the highest NT-proBNP levels. This suggests that independent mechanisms explain these unusually high levels. In one individual showing a high hs-TNT level, renal impairment may be at least partially to blame. We could make the assumption that our results highlight the existence of high and low responders for the cardiac biomarkers as for the CK.

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