The dynamics of cardiovascular biomarkers in recreational marathon runners

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The number of recreational athletes finishing marathons is increasing, but the data regarding the impact of endurance running on cardiovascular health are conflicting (1). Strenuous exercise may increase the circulating levels of cardiac biomarkers that are used to monitor heart health and disease. Here we examined the dynamics of a panel of cardiac biomarkers in a large population of recreational athletes who ran the Barcelona Marathon in 2016.

Levels of NT-proBNP, a surrogate marker of myocardial strain; ST2, which reflects extracellular matrix remodeling and fibrosis; and high-sensitivity troponin T (hs-TnT), which indicates myocyte injury were examined in 79 recreational athletes (72% men; mean age 39 ± 6 years; 71% ≥ 35 years). The participants responded to a call for volunteers (http://www.emmaroca.com/es/forms/estudi-cientific-perfil-de-ultrafondista/). Blood samples were collected at baseline (24-48 hours before the race), immediately after the race (1–2 hours after the race), and 48 hours post-race. Biomarkers were measured using commercially available assays. The local ethics committee approved the study, and all participants provided written informed consent.

The median (IQR) years of training and the weekly training hours were 7 (5–11) and 6 (5–8), respectively. The median (IQR) race time (hours:min:sec) was 3:32:44 (3:18:50–3:41:46). Echocardiographic indices were within normal ranges (LVEF 62 ± 5%, LVEDD 50 ± 5 mm; indexed LV mass 94 ± 20 g/BSA; TAPSE 26 ± 3 mm). Table 1 shows biomarker values. A significant number of athletes had ST2 and hs-TnT levels abnormally elevated (above accepted cut-off point for individuals without cardiac disease) at baseline and 48-hours post-race. Baseline hs-TnT was higher in women than men: 3.3 (2–7) vs. 2.1 (0.9–7.5); p=0.07; this correlated directly with weekly training hours (p=0.01) and correlated inversely with race completion time (p=0.009). None of
the biomarkers at baseline correlated with years of training; baseline NT-proBNP level correlated with age (p=0.007).

Table 1 shows the biomarker dynamics pre- and post-race. The blood levels of the three cardiac biomarkers increased significantly after the race, with 1.3-, 1.6-, and 16-fold increases in NT-proBNP, ST2, and hs-TnT, respectively; all p<0.001. NT-proBNP and ST2 levels returned to baseline 48 hours after the race, while the hs-TnT levels remained 60% higher than baseline levels (Table 1, p<0.001).

The hs-TnT increases were significantly higher in women than men (p=0.03) immediately after the race. Age and years of training showed no significant relationships with the dynamics of the biomarkers. However, we found an inverse relationship between weekly training hours and increased ST2 (p=0.007), and a direct relationship between race time and increased hs-TnT (p<0.001) and ST2 (p=0.05). In multivariable linear regression analyses that included age, sex, and variables with a p-value ≤0.1 in correlation analyses, race time remained independently associated with elevations in ST2 (p=0.03) and hs-TnT (p<0.001) levels.

To summarize, major distress affecting multiple cardiovascular pathobiological pathways occur up to 48 hours after a marathon race in a large population of recreational marathon athletes. Indeed, circulating hs-TnT and ST2 levels increased to abnormal levels and were significantly associated with worse athlete performance; by contrast, NT-proBNP was much less affected, likely mirroring athletes’ adaptation to hemodynamic load.

A recent study reported that minor increases in hs-TnT conferred long-term increased risk for myocardial infarction and cardiovascular death in individuals without symptoms of cardiovascular disease (2). Among our trained recreational athletes, the huge release of hs-TnT during the race together with persistently high circulating levels
post-race could indicate exercise-induced myocyte injury, possibly due to mechanisms such as volume or pressure overload, myocardial strain, or direct myocyte toxicity (3). It remains unclear whether hs-TnT increases in endurance athletes are harmful long-term for the cardiovascular system.

In a community-based cohort (the Framingham Offspring Study), ST2 was found to add prognostic value to standard risk factors for predicting death, overall cardiovascular events, and heart failure in otherwise healthy individuals (4). ST2 has also been shown to predict adverse outcomes and death in individuals with established heart failure (5). Endurance sport-driven ST2 increases in amateur runners might be responsible for long-term extracellular matrix remodeling and, ultimately, adverse ventricular remodeling.

Marathon running and other endurance sports are increasingly popular, raising concerns about sports-driven adverse ventricular remodeling and, in some cases, the development of patches of cardiac fibrosis that may be substrates for malignant arrhythmias. Should athletes with elevated cardiac biomarkers, in spite of normal imaging, be banned from endurance races? No evidence-based data support this at present, and more data and long-term follow-up are needed. Nevertheless, cardiac biomarkers, particularly hs-TnT and ST2, may emerge as Philippides surrogates, which are named for the Greek messenger who experienced sudden death after running more than 175 miles in two days.
References


Table 1. Cardiovascular biomarker dynamics in recreational marathon runners (n = 79)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Baseline</th>
<th>Immediately post-race</th>
<th>48 h post-race</th>
<th>p-value**</th>
<th>p-value***</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP, ng/L</td>
<td>70 (70–70)</td>
<td>92 (70–147)</td>
<td>70 (70–70)</td>
<td>&lt;0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>ST2, ng/mL</td>
<td>34.2 (24.7–40.9)</td>
<td>54.2 (38.2–72.4)</td>
<td>33.7 (28.9–42.3)</td>
<td>&lt;0.001</td>
<td>0.53</td>
</tr>
<tr>
<td>hs-TnT, ng/L</td>
<td>2.9 (1.7–7)</td>
<td>46.9 (24.1–91.1)</td>
<td>4.7 (2.4–8.85)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

≥cut-off point

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Baseline</th>
<th>Immediately post-race</th>
<th>48 h post-race</th>
<th>p-value**</th>
<th>p-value***</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP, ≥125 ng/L</td>
<td>0%</td>
<td>30.7%</td>
<td>1.4%</td>
<td>&lt;0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>ST2, ≥35 ng/mL</td>
<td>48.7%</td>
<td>86.7%</td>
<td>48.6%</td>
<td>&lt;0.001</td>
<td>0.99</td>
</tr>
<tr>
<td>hs-TnT, ≥14 ng/L</td>
<td>10.4%</td>
<td>88.3%</td>
<td>17.9%</td>
<td>&lt;0.001</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Values are reported as median (IQR); **1–2 h post-race vs. baseline; ***48 h post-race vs. baseline.