Cardiac Biomarkers, Electrolytes, and Other Analytes in Collapsed Marathon Runners

Implications for the Evaluation of Runners Following Competition

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Abstract

We measured analytes in collapsed Boston Marathon runners to compare with changes in asymptomatic runners. Of collapsed runners at the 2007 marathon, 18.2% had a measurable cardiac troponin T (cTnT) value with a mean postrace level of 0.017 ng/mL (0.017 µg/L; SD, 0.02 ng/mL [0.02 µg/L]). Three subjects had cTnT values above the cutoff (0.10 ng/mL [0.10 µg/L]) typically used for the diagnosis of acute myocardial infarction. The mean and median N-terminal pro-B-type natriuretic peptide levels were 73 ng/L (SD, 77.3 ng/L) and 54.3 ng/L (interquartile range, 22.8-87.3 ng/L), respectively, in collapsed runners. Only 4.9% had values more than the age-specific normal value (<125 ng/L for subjects younger than 75 years). In collapsed subjects at the 2006 marathon, 18.0% had an abnormal sodium value, including 18 cases of hypernatremia and 7 cases of hyponatremia. The ionized calcium level was low in 49% of subjects, and the ionized magnesium level was low in 19.5% and elevated in 1 subject. The blood lactate level was elevated in 95% of subjects.

The frequency of elevated postrace cTnT levels in collapsed athletes after endurance exercise is similar to that in asymptomatic runners. Other metabolic abnormalities, including hypernatremia, hyponatremia, low ionized calcium and magnesium levels, and lactic acidosis may contribute to muscle fatigue and collapse.

Although regular physical activity reduces future coronary heart disease events, episodes of vigorous exercise such as marathon running may precipitate acute coronary syndrome (ACS) and sudden death in 1 per 50,000 marathon participants.1-5 Prior studies of changes in cardiac troponin T (TnT) and I and B-type natriuretic peptide (BNP and N-terminal pro-B-type natriuretic peptide [NT-proBNP]) levels in asymptomatic runners who completed a marathon have demonstrated that mild to moderate elevations in levels of these markers are common without apparent ACS or heart failure.2,6-10 The mechanism of cardiac injury and myocyte stress reflected by elevation of troponin and B-type natriuretic peptide concentrations, respectively, remains under debate; however, presumably these elevations result from an incomplete myocardial adaptation to training in which vulnerable myocytes are selectively eliminated, particularly in athletes with lesser training.11 As well, the effects of endurance exercise on electrolyte and lactic acid concentrations as a function of collapse following exercise remains unclear.

In this study, we evaluated the levels of TnT, NT-proBNP, electrolytes, ionized calcium and magnesium, and lactate in collapsed marathon runners in the medical tent at the finish line of the 2006 and 2007 Boston marathons. Our hypothesis was that more prevalent abnormalities in cardiac biomarker, electrolyte, and lactic acid results would be noted in collapsed runners compared with asymptomatic runners.

Materials and Methods

All study procedures were approved by the McLean Hospital (Belmont, MA) Institutional Review Board. Heparinized blood samples were obtained from collapsed...
marathon runners admitted to the finish line medical tent at the 2006 and 2007 Boston marathons. Samples from the 2006 marathon were analyzed by whole blood point-of-care technologies for electrolytes, glucose, serum urea nitrogen, lactate, ionized calcium, and ionized magnesium using an acute care analyzer (Nova Biomedical, Waltham, MA).

After the 2007 marathon, discarded plasma samples were frozen at −80°C for subsequent analysis of TnT and NT-proBNP on the Roche Elecsys 2010 immunoassay analyzer (Roche Diagnostics, Indianapolis, IN) using a fourth-generation TnT assay and the standard Roche NT-proBNP assay. The cut point yielding the highest functional sensitivity at a 10% coefficient of variation for the TnT assay is 0.03 ng/mL (0.03 µg/L), and the appropriate age-matched upper limit of normal for the NT-proBNP assay for this population is less than 125 ng/L. The imprecision of the Roche NT-proBNP assay varies from less than 2.7% (within-run) to less than 3.2% (total imprecision) across the analytic range. Hemolyzed samples were excluded from the study.

The mean age of the subjects was 39.1 years (SD, 10.4 years). Of the subjects, 62% were men and 38% were women.

**Results**

Mean values for whole blood point-of-care chemistry analytes in collapsed marathon runners from the 2006 Boston Marathon are shown in Table 1. Not all analytes were measured for each subject owing to the availability of analyzers and samples for testing. Of 139 subjects, 25 (18.0%) had an abnormal sodium value; 18 cases showed hypernatremia and 7 showed hyponatremia. The serum urea nitrogen level was abnormal in 20 (49%) of 41. Of the subjects, 45 (51%) of 89 had a low ionized calcium level and 9 (22%) of 41 an abnormal ionized magnesium level that was low in 8 and elevated in 1 sample. Blood lactate levels were elevated in 75 (95%) of 79 cases and whole blood glucose levels in 43 (31%) of 139 cases, with no hypoglycemia noted.

The mean TnT value was 0.017 ng/mL (0.017 µg/L; SD, 0.02 ng/mL [0.02 µg/L]) in 99 collapsed marathon runners at the 2007 Boston Marathon. Of the 99 collapsed runners, 18 (18%) exhibited measurable levels of TnT and 8 (8%) had values of more than the threshold of 0.03 ng/mL (0.03 µg/L) indicative of myocardial necrosis by a fourth-generation TnT assay. Three subjects had TnT values of more than the traditional cutoff point of 0.1 ng/mL (0.1 µg/L) used for the diagnosis of acute myocardial infarction (0.106, 0.172, and 0.108 ng/mL [0.106, 0.172, and 0.108 µg/L]).

The median NT-proBNP value was 54 ng/L (interquartile range, 22.8–87.3 ng/L). Only 5 runners had NT-proBNP values of more than the age-adjusted cutoff value. These 5 values showed modest elevations of NT-proBNP (186, 188, 224, 221, and 331 ng/L). Of the 5 runners with an elevated NT-proBNP level, 3 (60%) also had measurable levels of TnT.

**Discussion**

Multiple studies reporting elevations in cardiac TnT and B-type natriuretic peptide (BNP or NT-proBNP) levels following marathon running clearly establish a myocardial source, further supported by recent data demonstrating strong associations between elevated cardiac biomarkers and the postrace develop-

**Table 1**

<table>
<thead>
<tr>
<th>Analyte</th>
<th>No. of Samples</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/L)</td>
<td>139</td>
<td>142.3</td>
<td>4.1</td>
<td>129.6</td>
<td>152.2</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>139</td>
<td>4.31</td>
<td>0.62</td>
<td>3.41</td>
<td>8.22</td>
</tr>
<tr>
<td>Ionized calcium (mmol/L)</td>
<td>89</td>
<td>1.09</td>
<td>0.07</td>
<td>0.9</td>
<td>1.22</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>134</td>
<td>45</td>
<td>3.4</td>
<td>37</td>
<td>55</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>139</td>
<td>117</td>
<td>37</td>
<td>58</td>
<td>294</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>79</td>
<td>3.45</td>
<td>1.61</td>
<td>1.1</td>
<td>11.2</td>
</tr>
<tr>
<td>Urea nitrogen (mg/dL)</td>
<td>41</td>
<td>19.76</td>
<td>4.2</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Ionized magnesium (mmol/L)</td>
<td>41</td>
<td>0.47</td>
<td>0.07</td>
<td>0.23</td>
<td>0.62</td>
</tr>
</tbody>
</table>

*Reference ranges are as follows: sodium, 135-147 mmol/L; potassium, 3.5-5 mmol/L; ionized calcium, 1.14-1.30 mmol/L; hematocrit: male, 41%-53%; female, 36%-46%; glucose, 70-110 mg/dL; lactate, <2 mmol/L; urea nitrogen, 8-25 mg/dL; and ionized magnesium, 0.47-0.65 mmol/L. Values for sodium, potassium, ionized calcium, lactate, and ionized magnesium are given in Système International (SI) units; conversions to conventional units are as follows: sodium (mEq/L), divide by 1.0; potassium (mEq/L), divide by 1.0; ionized calcium (mg/dL), divide by 0.25; lactate (mg/dL), divide by 0.111; ionized magnesium (mEq/L), divide by 0.50. Other values are given in conventional units; conversions to SI units are as follows: hematocrit (proportion of 1.0), multiply by 0.01; glucose (mmol/L), multiply by 0.0555; urea nitrogen (mmol/L), multiply by 0.357.

**Table 2**

<table>
<thead>
<tr>
<th>Troponin T Range, ng/mL (µg/L)</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.01 (&lt;0.01)</td>
<td>81 (62)</td>
</tr>
<tr>
<td>&gt;0.01 to &lt;0.03 (&lt;0.01 to &lt;0.03)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>0.03 to &lt;0.10 (0.03 to &lt;0.10)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>&gt;0.10 (&gt;0.10)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>
ment of abnormalities shown on 2-dimensional echocardiography. In a recent study of asymptomatic marathon runners following competition, more than 60% of participants had measurable increases in TnT levels, with 40% at or above the decision limit for acute myocardial necrosis (TnT ≥0.03 ng/mL [0.03 µg/L]). These changes were inversely related to training experience. In another recent study, postrace cardiac TnT levels were elevated (≥0.01 or ≥0.1 ng/mL [0.01 or 0.1 µg/L]) in 68% of 482 runners following the 2002 Boston Marathon, including 11% with a TnT level of 0.075 ng/mL (0.075 µg/L) or more or of 0.5 ng/mL (0.5 µg/L) or more.

In contrast with these results in asymptomatic runners who completed a marathon, in our study, only 18% of collapsed runners showed measurable TnT values, with 8% greater than 0.03 ng/mL (0.03 µg/L); 3 had values of more than 0.1 ng/mL (0.1 µg/L). These percentages are distinctly lower than those observed by Neilan et al and Fortescue et al in asymptomatic runners. Because the degree of TnT release seems to somewhat parallel the degree of endurance exercise, it may be that our collapsed runners did not achieve the intensive myocardial stress achieved by runners who complete a full marathon. Lending further support to this concept is that the values for NT-proBNP in collapsed runners in our study were generally within the age-adjusted normal range and lower than the median postrace NT-proBNP level of 131 pg/mL reported in asymptomatic runners who successfully completed the race. Thus, in aggregate, our data suggest that cardiovascular insufficiency does not underlie the mechanism of collapse in the vast majority of collapsed runners.

Rapid whole blood point-of-care analyte results in 135 collapsed runners at the 2006 race demonstrated frequent abnormalities of sodium, lactate, ionized calcium, and ionized magnesium levels. Hypernatremia was observed in 13% and hyponatremia in 5% of collapsed marathon runners (compared with 25% and 6%, respectively, during the 2004 race at warmer temperatures). Prevention of hypernatremia and hyponatremia is the focus of recently revised recommendations for optimal hydration issued by the American College of Sports Medicine and the International Marathon Medical Directors Association. The former guidelines emphasize preventing dehydration in higher performance athletes by advice to drink “ahead of thirst,” and the latter stress drinking to thirst only to minimize the risk of overhydration, especially in slower marathon runners and walkers.

Elevated levels of whole blood lactate were observed in 95% of collapsed runners. Of these, 32 (40.5%) had values more than the range commonly regarded as a “critical value” (31.5 mg/dL [3.5 mmol/L]). Of the subjects, 51% had a low ionized calcium level and 23% an abnormal ionized magnesium level (8 of 9 had hypomagnesemia). The low ionized calcium values are most likely a consequence of the elevations in lactate because lactic acidosis is known to decrease the ionized calcium level. Metabolic acidosis also is a known cause of hypomagnesemia, as was found in 8 cases. Low ionized calcium and magnesium levels may contribute to impaired skeletal muscle and, potentially, myocardial function in the collapsed runners. The mean glucose value of 117 mg/dL (6.5 mmol/L) in collapsed runners reported herein is similar to the mean of 110 mg/dL (6.1 mmol/L) reported in asymptomatic finishers. No collapsed runners were hypoglycemic.

The mechanism underlying exertional triggering of acute cardiac events remains unknown. Relative risks 2.38- and 16.9-fold greater in apparently healthy women and men, respectively, have been reported for acute cardiac events, including sudden death, during strenuous exercise compared with baseline at rest. Marathon running is associated with an abrupt but transient increase in relative risk for ACS in persons who are otherwise at relatively low risk. Despite improved emergency cardiac care along race courses in recent years, the rate of sudden death predominantly in middle-aged men has remained at 1 per 50,000 marathoners during the last 2 decades. The Marine Corps and Los Angeles marathons experienced multiple cases of cardiac arrest in 2007, perhaps reflecting increasing participation of older runners. Boston Marathon entrants between ages 40 and 59 years increased from 4,000 in 1997 to 10,000 in 2007.

Although we show comparable (if not lower) levels of diagnostic and prognostically meaningful cardiac biomarkers among endurance athletes compared with levels in athletes who finished the marathon, we also found prevalent abnormalities in various electrolytes, which in conjunction with lactic acidosis and a decrease in ionized calcium and magnesium levels may contribute to the enhanced risk for ventricular fibrillation during acute exertional events. Furthermore, the significance of these metabolic abnormalities as related to exercise-induced collapse is not yet clear.

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References

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