Body Composition, Hemodynamic, and Biochemical Parameters of Young Female Normal-Weight Oligo-Amenorrheic and Eumenorrheic Athletes and Nonathletes

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Key Words

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Abstract

Aims: Low-weight hypogonadal conditions such as anorexia nervosa are associated with marked changes in body composition, hemodynamic and hematological parameters, and liver enzymes. The impact of athletic activity in normal-weight adolescents with/without amenorrhea on these parameters has not been assessed. Our aim was to examine these parameters in normal-weight athletes and nonathletes and determine any associations with body composition, oligo-amenorrhea, and exercise intensity. **Methods:** We assessed vital signs, complete blood counts, liver enzymes, and regional body composition in 43 oligo-amenorrheic athletes (OAA), 24 eumenorrheic athletes (EA), and 23 nonathletes aged 14–21 years. **Results:** The BMI was lower in OAA than in EA. Systolic and pulse pressure and temperature were lowest in OAA. Blood counts did not differ among groups. Aspartate aminotransferase (AST) was higher in both groups of athletes, while alanine aminotransferase

(ALT) was higher in OAA than in EA and nonathletes. Total and regional fat were lower in OAA than in other groups, and these factors were associated positively with heart rate and inversely with liver enzymes. **Conclusions:** Athletic activity is associated with higher AST levels, whereas menstrual dysfunction is associated with lower total and regional fat and higher ALT levels. Higher liver enzymes are associated with reductions in total and regional fat.

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Introduction

The number of young women participating in athletics has increased markedly in recent decades [1]. Exercise has many benefits but carries risks of energy deficit when excessive [2, 3]. The female athlete triad of low energy availability, menstrual dysfunction, and low bone mineral density is now increasingly recognized [4], with ~24% of adolescent athletes demonstrating menstrual dysfunction [5]. While excessive exercise has known associations with adverse reproductive and bone outcomes [3, 6], there are few data regarding other adverse effects of excessive exercise and amenorrhea.

Conditions of extreme undernutrition, such as anorexia nervosa (AN), are characterized by changes in body composition, hemodynamic and hematological parameters, and liver enzymes [7, 8]. Changes in heart rate, systolic blood pressure (SBP), and blood flow are also described in adult amenorrheic athletes [9]. However, the impact of exercise and oligo-amenorrhea in normal-weight adolescent athletes is not known. We have shown that adolescent oligo-amenorrheic athletes (OAA) (even when normal weight) have reductions in body fat that differentiate them from eumenorrheic athletes (EA) and nonathletes [10]. The associations of a reduced fat mass with hemodynamic, hematological, and biochemical parameters in this population remain to be determined.

Regular exercisers have a lower heart rate, SBP, and diastolic blood pressure (DBP) than nonexercisers [11, 12] due to their enhanced parasympathetic tone [13]. Similar changes are observed with severe energy deprivation, as in AN [8]. However, data are lacking regarding hemodynamic parameters in young adolescent normal-weight OAA compared to EA, particularly in relation to body fat. Also, blood counts may decrease with extreme undernutrition (such as in AN) [8, 14]. Studies have not examined hematological parameters in normal-weight adolescent OAA versus EA, although studies in adult athletes report a high prevalence of dilutional pseudoanemia in this population [reviewed in 15]. Finally, although most athletes do not have significant biochemical abnormalities on pre-screening evaluations [16], their liver enzymes are sometimes elevated. In fact, liver enzymes are elevated at the extremes of the nutritional spectrum, in fatty liver disease from visceral adiposity [17] and related to malnutrition in AN [7, 18]. Data are lacking regarding associations of chronic exercise and amenorrhea with liver enzymes in relation to body fat (a surrogate for energy stores).

Our objective was to examine hemodynamic and hematologic parameters and liver enzymes in normal-weight athletes and nonathletes aged 14–21 years and determine the associations of body composition, oligo-amenorrhea, and intensity of exercise with these parameters. We hypothesized that OAA would have greater impairment of these parameters than EA and nonathletes related to their lower body fat (a reflection of energy stores).

Methods

Subjects were recruited from medical clinics, newspapers, and colleges. We enrolled 43 OAA, 24 EA, and 23 nonathletes aged 14–21 years. The training criteria for athletes were ≥ 20 miles/week

of running or ≥ 4 h/week of weight-bearing training for ≥ 6 months in the past year. The inclusion criteria for nonathletes were < 2 h/week of weight-bearing activity. Oligo-amenorrhea was defined as the absence of menses for at least 3 months within a ≥ 6 -month period of oligomenorrhea (cycle length > 6 weeks) or the absence of menarche at > 16 years. Three subjects aged 15.1–16.8 years had not attained menarche, and other causes of menarchal delay were ruled out. Eumenorrhea was defined as ≥ 9 menses (cycle length 21–35 days) in the previous year. All subjects had a bone age ≥ 14 years and BMI between the 10th and 90th percentiles. Other causes of amenorrhea such as medications affecting the hypothalamic-pituitary-ovarian axis (including oral contraceptives and hormone replacement), hyperprolactinemia, ovarian failure, polycystic ovary syndrome, and thyroid dysfunction were ruled out. This study was approved by the Partners HealthCare Institutional Review Board. Informed consent was obtained from subjects aged ≥ 18 years and the parents of subjects aged < 18 years. Informed assent was obtained from girls < 18 years.

Weight was measured on a single electronic scale with subjects wearing a hospital gown, and height was recorded as an average of 3 measurements on a single wall-mounted stadiometer. BMI was calculated as weight (kg)/height (m)². The percent ideal body weight was calculated using the BMI percentile method. Bone age was assessed from a left-hand radiograph [19]. A detailed exercise history was obtained to calculate the activity level (h/week of athletic activity over 12 months). Resting energy expenditure (REE) was measured by indirect calorimetry (VMAX Encore 29 metabolic cart; Viasys Healthcare, San Diego, Calif., USA). Blood pressure was measured using an aneroid sphygmomanometer after adjusting the cuff size in a sitting position. Pulse pressure was calculated as the difference between the SBP and the DBP. Pulse was measured manually and temperature with an infrared tympanic thermometer in a standardized fashion. Complete blood counts were analyzed in the hospital laboratory (Sysmex® X-series analyzer), and potassium and liver function were assessed by LabCorp using standard methods (Roche/Hitachi MODULAR® P/D Analyzers). All subjects were interviewed by the study psychologist for disordered eating behavior and were administered two questionnaires to assess eating behaviors, i.e. the Eating Disorders Inventory-2 and the Three-Factor Eating Questionnaire.

Waist and hip measurements were taken standing using a plastic tape measure to the nearest 0.1 cm at the end of expiration. The waist-to-hip ratio was calculated as the waist measurement at the iliac crest divided by the greatest hip circumference. We used dual energy X-ray absorptiometry (Hologic Discovery A; Waltham, Mass., USA; software version APEX 3.3) to measure the percent body fat and regional fat and the lean mass. Trunk/extremity fat was calculated by dividing trunk fat by total extremity fat. The coefficients of variation for lean and fat mass were 1.0 and 2.1%.

Statistical Methods

JMP Software (v10; SAS Institute, Inc., Cary, N.C., USA) was used for analysis. Results are reported as means $\pm$ SD. We used ANOVA to determine differences among groups for most parameters, followed by the Tukey-Kramer test to control for multiple comparisons. For nonnormally distributed parameters (AST, ALT, alkaline phosphatase, fat mass, and trunk fat) a nonparametric analysis (Kruskal-Wallis) was used followed by the Steel-Dwass test to control for multiple comparisons. Subjects were also divided into quartiles based on hours per week of exercise activity, and

Table 1. Clinical characteristics of amenorrheic athletes, EA, and nonathletes

Characteristics	OAA (n = 43)	EA (n = 24)	NA (n = 23)	p	p OAA vs. EA	p OAA vs. NA	p EA vs. NA
Age, years	19.2 (2.1)	18.0 (2.1)	19.1 (1.7)	0.052	–	–	–
Bone age, years	17.5 (1.0)	17.2 (1.2)	17.5 (1.1)	NS	–	–	–
Age of menarche, years	13.7 (1.8)	12.8 (1.4)	12.2 (1.5)	0.0012	0.06	0.001	–
Duration of amenorrhea, m	9.0 (13.2)						
Tanner stage (breast)	4.6 (0.7)	4.7 (0.6)	4.8 (0.6)	NS	–	–	–
Height, cm	165.5 (6.9)	165.8 (8.2)	162.8 (7.2)	NS	–	–	–
Weight, kg	56.3 (7.1)	62.0 (10.7)	57.7 (8.0)	0.03	0.027	–	–
BMI, kg/m ²	20.6 (2.1)	22.4 (2.4)	21.7 (2.5)	0.005	0.005	–	–
Percent ideal body weight	96.4 (9.7)	107.8 (13.8)	102.6 (13.3)	0.001	0.0008	–	–
Activity level, h/week	9.9 (4.9)	11.0 (4.3)	1.0 (1.4)	<0.0001	–	<0.0001	<0.0001
REE, cal	1,255 (188)	1,444 (219)	1,255 (193)	0.0007	0.001	–	0.004
<i>Regional body composition</i>							
Waist circumference, cm	72.6 (6.0)	75.4 (7.3)	74.7 (7.1)	NS	–	–	–
Hip circumference, cm	91.2 (5.2)	94.5 (7.5)	91.9 (6.1)	NS	–	–	–
Body fat, %	21.3 (5.4)	23.5 (3.8)	27.0 (5.2)	0.0001	–	<0.0001	0.04
Total fat mass ^a , kg	12.4 (3.8)	15.1 (4.4)	16.0 (4.9)	0.006	0.02	0.004	–
Trunk fat ^a , kg	4.7 (1.8)	5.6 (2.2)	5.7 (2.1)	0.051	0.07	0.028	–
Extremity fat, kg	6.8 (2.1)	8.6 (2.3)	9.4 (3.0)	0.0002	0.004	0.0001	–
Trunk-to-extremity fat ratio	0.7 (0.2)	0.6 (0.1)	0.6 (0.1)	NS	–	–	–
Total lean mass, kg	43.5 (5.6)	46.3 (7.7)	40.5 (4.4)	0.005	–	–	0.003
Total extremity lean mass, kg	19.2 (2.8)	21.0 (3.9)	18.2 (2.6)	0.01	0.026	–	0.003

Values are expressed as means (SD). p values ≤0.1 are reported. NS = Not significant. ^a Nonparametric testing.

variables were compared across quartiles of activity. We used Spearman's correlations to determine associations between variables, and multivariate analysis to control for confounders. Regression modeling was performed to determine predictors of liver enzymes, with a p value of 0.1 to enter and leave the model. We included hours/week of athletic activity, percent body fat, lean mass amenorrhea, and duration as covariates. $p < 0.05$ was considered statistically significant.

Results

Clinical Characteristics

Groups did not differ in terms of chronologic age, bone age, height, or Tanner stage (table 1). OAA had a lower BMI than EA, although all subjects had a BMI >17.5 (BMI between the 10th and the 90th percentiles). OAA had a later menarchal age than nonathletes. Thirty-five percent of OAA reported disordered eating compared to 4.2% of EA and none of the nonathletes ($p = 0.0008$). Activity level was higher in athletes versus nonathletes per protocol and did not differ between OAA and EA. REE was highest in EA, even after adjusting for lean mass.

Regional Body Composition

Waist and hip circumferences did not differ across groups (table 1). Both athlete groups had lower percent body fat values than nonathletes. Total and extremity fat were lower in OAA than in EA and nonathletes. Trunk fat was lower in OAA than in nonathletes and trended lower than in EA. However, after adjusting for total fat, OAA had higher trunk fat ($p = 0.006$) values, lower extremity fat ($p = 0.002$) values, and a higher trunk/extremity fat ratio ($p = 0.004$) than the other groups. EA had higher total and extremity lean masses than OAA and nonathletes.

Hemodynamic, Hematological, and Biochemical Parameters

Heart rate was lower in athletes than in nonathletes (table 2) but did not differ in OAA versus EA. SBP and pulse pressure were lower in OAA than in EA but did not differ from nonathletes. DBP did not differ among groups. Heart rate was significantly different when athletic activity quartiles were compared ($p = 0.0001$), and girls in each of the upper 3 quartiles had a lower heart rate than those in the first quartile. No relationship was

Table 2. Hemodynamic, hematological, and biochemical parameters of amenorrheic athletes, EA, and nonathletes

	OAA (n = 43)	EA (n = 24)	NA (n = 23)	p	p OAA vs. EA	p OAA vs. NA	p EA vs. NA
<i>Hemodynamic characteristics</i>							
SBP, mm Hg	100.4 (8.7)	107.5 (6.7)	103.0 (7.9)	0.003	0.002	–	–
DBP, mm Hg	66.6 (7.6)	67.2 (7.3)	66.0 (6.9)	NS	–	–	–
Pulse pressure, mm Hg	33.7 (6.2)	40.3 (6.4)	36.9 (7.5)	0.001	0.0006	–	–
Heart rate, beats/min	57.5 (9.9)	60.7 (10.1)	71.3 (10.2)	<0.0001	–	<0.0001	0.001
Temperature, °F	97.6 (0.9)	98.4 (0.6)	98.4 (0.9)	0.0002	0.002	0.001	–
<i>Hematological characteristics</i>							
WBC, $\times 10^3/\mu\text{l}$	5.6 (1.4)	6.1 (1.5)	6.3 (1.6)	NS	–	–	–
RBC, $\times 10^6/\mu\text{l}$	4.2 (0.3)	4.3 (0.3)	4.4 (0.3)	NS	–	–	–
Hemoglobin, g/dl	13.1 (0.9)	13.2 (1.0)	13.1 (0.7)	NS	–	–	–
Hematocrit, %	38.6 (2.9)	39.2 (3.4)	38.8 (2.0)	NS	–	–	–
MCV, fl	91.1 (5.3)	90.7 (6.2)	89.2 (3.2)	NS	–	–	–
MCH, pg	30.8 (1.9)	30.6 (2.2)	30.1 (1.2)	NS	–	–	–
MCHC, g/dl	33.9 (0.8)	33.8 (1.3)	33.8 (0.9)	NS	–	–	–
RDW, %	13.5 (1.0)	13.2 (0.7)	13.4 (0.7)	NS	–	–	–
<i>Biochemical characteristics</i>							
Potassium, mmol/l	4.1 (0.4)	4.3 (0.4)	4.2 (0.4)	NS	–	–	–
Total protein, mg/dl	7.1 (0.5)	7.2 (0.4)	7.3 (0.3)	NS	–	–	–
Albumin, mg/dl	4.6 (0.3)	4.5 (0.2)	4.5 (0.2)	NS	–	–	–
Total bilirubin, mg/dl	0.4 (0.3)	0.4 (0.2)	0.4 (0.2)	NS	–	–	–
Direct bilirubin, mg/dl	0.1 (0.1)	0.1 (0.1)	0.1 (0.04)	NS	–	–	–
Alkaline phosphatase ^a , U/l	70.1 (23.4)	72.8 (17.3)	63.0 (16.6)	NS	–	–	–
AST ^a , U/l	26.5 (9.0)	26.7 (10.3)	18.6 (4.4)	0.0001	–	<0.0001	0.0008
ALT ^a , U/l	23.7 (12.6)	16.7 (7.7)	14.0 (4.8)	<0.0001	0.0006	<0.0001	–

Values are expressed as means (SD). MCV = Mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red cell distribution width. ^a Nonparametric testing.

found between activity level and SBP, DBP, or pulse pressure. Temperature was lower in OAA than in EA and nonathletes, and it was not affected by the date of screening (seasonal variation).

Groups did not differ in terms of hematological parameters, albumin, or total protein. However, 3 OAA and 2 EA had hematocrit <34.8% (mean – 2 SD for controls). Aspartate aminotransferase (AST) was elevated in both groups of athletes compared to nonathletes, and alanine aminotransferase (ALT) was higher in OAA versus EA and nonathletes; 9.3, 8.7, and 0% of OAA, EA, and nonathletes, respectively, had AST levels above the normal range, and 18.6, 0, and 0% of OAA, EA, and nonathletes, respectively, had ALT levels above the normal range. After adjusting for hours/week of athletic activity, the difference in AST across groups was not significant. However, ALT remained higher in OAA compared to the other groups. Total bilirubin, direct bilirubin, and alkaline phosphatase did not differ among groups.

Determinants of Hemodynamic, Hematological, and Biochemical Parameters

SBP and DBP were positively associated with BMI (table 3). Heart rate was positively associated with percent body fat and total, trunk, and extremity fat and inversely associated with lean mass and athletic activity. Duration of amenorrhea inversely predicted SBP, pulse pressure, heart rate, and temperature.

AST and ALT were associated inversely with fat stores (percent body fat and total, trunk, and extremity fat) and positively with athletic activity level, with AST having a stronger correlation than ALT. We found a positive association between AST and total and extremity lean mass. In addition, menarchal age and amenorrhea duration were positive predictors of liver enzymes. WBC counts were positively associated with BMI ($r = 0.23$, $p = 0.03$), whereas RBC counts were inversely associated with duration of amenorrhea ($r = -0.29$, $p = 0.006$).

Table 3. Correlations of body composition with hemodynamic parameters and liver enzymes

	SBP		DBP		Pulse pressure		Pulse		Temperature		AST		ALT	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Menarchal age, years	0.02	–	0.0	–	–0.06	–	–0.16	–	–0.16	–	0.28	0.009	0.24	0.02
Duration of amenorrhea, months	–0.25	0.02	0.04	–	–0.39	0.0003	–0.23	0.04	–0.27	0.01	0.24	0.03	0.38	0.0003
Athletic activity, h/week	0.11	–	0.07	–	0.07	–	–0.36	0.0006	–0.18	–	0.38	0.0002	0.26	0.01
BMI, kg/m ²	0.30	0.005	0.32	0.003	0.06	–	0.17	–	0.16	–	–0.07	–	–0.15	–
Percent body fat	0.04	–	0.17	–	–0.09	–	0.37	0.0002	0.15	–	–0.44	<0.0001	–0.33	0.001
Total fat, kg	0.10	–	0.19	–	–0.06	–	0.28	0.008	0.11	–	–0.35	0.0008	–0.31	0.003
Trunk fat, kg	0.09	–	0.21	0.046	–0.08	–	0.24	0.02	0.05	–	–0.31	0.003	–0.24	0.02
Extremity fat, kg	0.13	–	0.17	–	–0.01	–	0.33	0.002	0.19	0.08	–0.36	0.0005	–0.36	0.0005
Total lean mass, kg	0.06	–	0.05	–	–0.03	–	–0.32	0.003	–0.12	–	0.28	0.008	0.19	0.07
Total extremity lean mass, kg	0.10	–	0.10	–	–0.03	–	–0.25	0.02	–0.09	–	0.25	0.02	0.14	–

p values ≤0.1 are reported. Spearman's correlations are reported.

Reported differences among groups remained significant after controlling for athletic activity, percent body fat, lean mass, and amenorrhea duration. Significant predictors of AST were subject group (EA and OAA vs. nonathletes) and percent body fat, contributing to 24% of the variability. The only predictor for ALT was subject group (OAA vs. EA and nonathletes), explaining 16% of the variability.

Discussion

With increasing participation of young women in athletics, there is increasing awareness of the female athlete triad, a key component of which is suboptimal energy availability, leading to menstrual dysfunction. All cellular processes including growth, thermoregulation, and reproduction require energy, and in energy deficit states the available energy is directed towards crucial life-sustaining functions such as temperature and glucose homeostasis. This is consistent with extreme energy depletion (as in AN) causing alterations in hemodynamic, hematological, and biochemical parameters [8]. We report differences in body composition, hemodynamic, and biochemical parameters in normal-weight adolescent OAA compared to EA and nonathletes.

Regional Body Composition

EA had a lower percent body fat and a higher lean mass than nonathletes, consistent with the known effects of endurance training on body composition [20]. Disordered

eating is common in athletes [21], and with excessive exercise it increases the risk of low energy availability. Thirty-five percent of our normal-weight OAA reported disordered eating, which may explain the lower BMI and percent ideal body weight in OAA compared to EA (though OAA did not differ from nonathletes). Moreover, OAA had lower total and regional fat than the other groups, indicative of an overall reduction in energy stores (despite a normal weight).

Interestingly, after controlling for total fat, OAA had higher trunk fat and trunk/extremity fat than EA and nonathletes, suggestive of a central fat redistribution in normal-weight OAA. This is in contrast to low-weight AN girls who have reductions in trunk fat and trunk/extremity fat relative to total fat [8, 22]. Thus, the severe energy depletion (as in AN) that causes severe weight loss likely has a different effect on fat distribution than less severe energy depletion where weight is preserved (as in normal-weight OAA). In a previous study, we reported that OAA have higher cortisol than EA and nonathletes [23]. Because increased cortisol favors central adiposity [24, 25], it is possible that trunk fat redistribution in OAA is at least partially mediated by increased cortisol. This is consistent with the increased trunk fat reported following weight gain in women with AN with higher baseline cortisol levels [26–28]. The absence of truncal adiposity in active AN (despite high cortisol) is likely from direct lipolytic effects of increased growth hormone (from low IGF-1 and reduced negative feedback) [27, 29]. Normal-weight OAA do not have the marked reductions in IGF-1 seen in AN [8, 30], and thus growth hormone levels are

likely not as high as in AN. We did not assess cortisol associations with body composition, and this warrants further investigation.

Hemodynamic Parameters

Long-term endurance exercise decreases the heart rate and blood pressure [11, 31] due to intrinsic cardiac remodeling and increased parasympathetic tone [32]. Our findings are consistent in that EA and OAA had a lower heart rate than nonathletes. Heart rate was inversely associated with activity [33] and positively associated with body fat, which may indicate an adaptation to conserve energy rather than a physiological response to exercise.

Exercise has the beneficial effect of lowering blood pressure by reducing vascular resistance and decreasing sympathetic activity [11, 12]. Studies have reported a lower SBP in adult OAA compared to EA [9, 34]. In our study, OAA had a lower SBP than EA; however, this was not associated with activity. A difference in SBP among normal-weight young athletes with similar athletic activity (OAA and EA) suggests that factors other than exercise may drive the hemodynamic response in OAA. Heart rate and blood pressure are predicted by body fat in AN, a state of extreme energy deficit [8]. However, we found no association between fat mass and SBP in normal-weight athletes and nonathletes. We did find an inverse association between SBP and duration of amenorrhea, consistent with reported associations of hypoestrogenism, with a lower blood pressure and heart rate in exercisers [9]. Thus, the low SBP in OAA may be mediated by menstrual dysfunction and hypoestrogenism rather than by exercise or nutritional deficit.

To our knowledge, this is the first study to assess associations of oligo-amenorrhea and lower fat stores with body temperature in OAA. Klentrou et al. [35] showed that thermoregulation was affected by hormonal status and fat mass in premenarcheal and eumenorrheic young girls. We found lower temperatures in OAA versus EA and nonathletes associated with amenorrhea duration, suggesting efforts towards energy conservation in OAA.

Resting Energy Expenditure

EA had higher REE than OAA and nonathletes, even after controlling for lean mass. In nonathletes, an inverse association is expected between REE and parasympathetic activity [36], whereas in athletes, a paradoxical positive association is reported, implying higher REE at lower heart rates and blood pressures [13]. In our study, EA demonstrated athletic adaptive changes (a higher REE with a lower heart rate), indicating optimum exercise

benefits. In contrast, despite a normal weight, similar activity, and enhanced parasympathetic activity, OAA had lower REE than EA, likely an additional adaptive measure to conserve energy and prevent weight loss.

Hematological Parameters

Information about hematologic changes in adolescent regular training athletes is limited. One study reported abnormal findings during routine screening in 51% of athletes, such as reduced hematocrit and increased WBC counts [37]. In fact, dilutional pseudoanemia is a common finding in adult elite endurance athletes consequent to plasma volume expansion [15]. We did not find differences in hematological parameters among groups, which may reflect the younger age of our subjects or a lower intensity of training. This differed from AN girls, who have alterations in many hematological parameters associated with lower BMI [8]. In our study, OAA had WBC counts within the low normal range were positively associated with BMI. There is evidence of transitory leukocytosis and decreased hematocrit following intense short-term exercise; however, long-term alterations have not been reported [38, 39]. We conclude that chronic exercise and oligo-amenorrhea in young athletes do not affect hematological parameters when weight is preserved.

Biochemical Parameters

We also assessed associations of endurance training, hypogonadism, and low body fat with liver enzymes. Aminotransferases are markers of liver injury; ALT elevation is more specific to hepatic cell damage, whereas AST may increase with muscular injury as in myocardial infarction or myolysis [40]. One study reported increased AST (27%) and bilirubin (12%) during routine biochemical screening in elite athletes [16]. Intense short-term exercise can cause AST elevation (sparing ALT) [41]; however, the effects of chronic exercise on liver enzymes remain unclear. In addition, elevated liver enzymes have been reported in AN consequent to malnutrition [7, 18], and inverse associations of ALT and GGT with BMI and body fat have been found [42]. We thus expected elevated AST in athletes related to activity, and elevated ALT in OAA from energy depletion (indicated by lower body fat).

Consistent with our expectations, AST was elevated in both groups of athletes compared to nonathletes, and ALT (more predictive of hepatocyte injury) was higher in OAA than in EA and nonathletes. In fact, 18.6% of OAA had ALT levels above normal. Differences between groups

persisted after controlling for confounders. Both transaminases were inversely associated with body fat in normal-weight subjects, consistent with data in AN [42]. In a regression model, body fat and being an athlete (OAA and EA vs. nonathletes) were predictors of AST, while being amenorrheic (OAA vs. EA and nonathletes) was the only predictor of ALT. AST had a stronger association with activity level, and ALT with amenorrhea duration. We thus speculate that ALT elevations are related to the nutritional and hormonal state of OAA (low fat stores and amenorrhea duration), whereas AST elevations are from the muscular workload (athletic activity). This indicates that ALT elevations are more concerning in athletes than AST elevations and suggest poorer nutrition and a risk of hypogonadism.

In conclusion, athletic activity is associated with lower body fat and heart rate and elevated AST. Oligo-amenorrhea is associated with reductions in body fat, SBP, and body temperature and elevations in ALT. Our data sug-

gest that body weight provides limited information about nutritional status in athletes. OAA may have altered metabolic and endocrine function despite being normal weight and need careful monitoring of hemodynamic parameters and liver enzymes. A trend over time of decreasing heart rate and increasing liver enzymes may indicate reductions in body fat (and thus energy stores) and should trigger discussions of caloric intake to keep pace with the exercise energy expenditure.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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