

# THE INFLUENCE OF A SINGLE BOUT OF WRESTLING EXERCISE ON SERUM LEVELS OF ISCHEMIA-MODIFIED ALBUMIN

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The purpose of this study was to investigate the effect of single bouts of exercise on changes in ischemia-modified albumin (IMA). Twenty wrestlers (mean age,  $28.8 \pm 8.96$  years) participated in this study. They performed a typical 1.5-hour wrestling training session. Blood was sampled before and immediately after training. The albumin-cobalt binding test was used to measure IMA levels. Serum albumin concentrations and blood lactate levels were also evaluated. Mean serum IMA levels were  $0.281 \pm 0.052$  ABSU before training and  $0.324 \pm 0.039$  ABSU after training. A single bout of acute exercise led to significant ( $p < 0.05$ ) increases in IMA. The results of the correlation tests indicated that there was a positive correlation between IMA and lactate levels ( $r = 0.873$ ;  $p < 0.001$ ). There were no significant correlations between IMA and albumin ( $r = -0.058$ ;  $p = 0.807$ ), and between albumin and lactate levels ( $r = -0.120$ ;  $p = 0.613$ ). Our results showed that demanding, intense anaerobic physical activity might influence the generation of IMA. [*J Exerc Sci Fit* • Vol 8 • No 2 • 67-72 • 2010]

**Keywords:** exercise, ischemia-modified albumin (IMA), wrestlers

## Introduction

The measurement of ischemia-modified albumin (IMA) by the albumin-cobalt binding (ACB) test is a new biomarker of cardiac ischemia, skeletal muscle ischemia and cerebral ischemia (Gunduz et al. 2008; Roy et al. 2004; Bar-Or et al. 2000). In the acute ischemic condition, the metal-binding capacity of albumin for transition metals, such as copper, nickel and cobalt, is reduced, generating a metabolic variant of the protein, commonly known as IMA (Gunduz et al. 2008). Although the precise mechanism for IMA production remains unknown,

ischemia may lead to a site-specific modification of the N terminus of albumin (Abboud et al. 2008; Sadler et al. 1994). Ischemic conditions in tissue may stimulate the degradation of the N terminus of albumin and hence result in elevated IMA values.

The influence of exercise on a number of cardiac biomarkers, including markers of inflammation, cardiac function, necrosis and ischemia, has been studied previously. Exercise-related increase in cardiac biomarkers has been demonstrated in elite athletes (Scharhag et al. 2008; Middleton et al. 2006; Apple et al. 2002; Neumayr et al. 2001). Recent studies have suggested that acute bouts of ultraendurance exercise may result in the appearance of biomarkers of cardiac cell damage in the systemic circulation and the release of cardiac-specific proteins as an indication of subclinical myocardial damage (Whyte 2008; Middleton et al. 2006; Apple et al. 2002; Neumayr et al. 2001). IMA is



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regarded to be a promising cardiac biomarker. The elevation of IMA has been proposed to reflect ischemic insult to cardiac tissue (Scharhag et al. 2008). On the other hand, IMA increases are not always associated with myocardial ischemia, but could be attributed to either gastrointestinal ischemia or skeletal muscle ischemia (Apple et al. 2002).

In the present study, wrestling was chosen because it consists of a form of exercise that demands power, endurance and strength. The general physiological profile of the successful wrestler is one of high anaerobic power, high anaerobic capacity and high muscular endurance (Horswill 1992). Observation of the intensity of wrestling reveals that the anaerobic component is of vital concern. The sources of energy for a wrestler's quick and explosive maneuvers are the phosphagens (ATP-PC) and glycogen (anaerobic glycolysis). In terms of biochemistry, the capacity of muscle to maintain maximum power for this duration of time is thought to be due to its capacity to undergo anaerobic glycolysis, buffer metabolic acids, and aerobically metabolize fuel for energy (Yoon 2002). Anaerobic exercise results in a transient and acute muscular deoxygenation, which resembles the ischemia-reperfusion syndrome (Groussard et al. 2003; Nioka et al. 1998). Thus, the relationship between anaerobic pathways for energy metabolism during strenuous anaerobic training and cardiovascular changes need to be investigated.

To our knowledge, there are no studies assessing IMA levels following high-intensity anaerobic exercise. Assessment of IMA may provide an opportunity to examine the utility of IMA in an exercise setting. Therefore, the aim of the present study was to investigate the effects of intense exercise on IMA levels in wrestlers.

## Methods

### Participants

Twenty healthy wrestlers from a top ranking team in the Turkish Wrestling Federation First League volunteered to participate in this study. They were all freestyle wrestlers competing in national and international competitions. The study was approved by the local research ethics committee of our faculty and all the athletes gave written informed consent before participating. The mean age of the wrestlers was  $28.8 \pm 8.96$  years. Table I displays the physical characteristics of the athletes. Each participant served as his own control. According to a detailed health questionnaire and clinical examination, the athletes were free of cardiovascular disease.

### Field study

A single bout of wrestling exercise was held approximately 2 weeks before the end of the wrestling season. At the time of the study, the athletes had been undergoing six training sessions of 90 minutes each every week. In this study, the athletes undertook a 1.5-hour intense session of anaerobic exercises, which comprised the following:

- warm-up: jogging and sports-specific stretch exercises (20 minutes);
- medicine ball drills (10 minutes);
- wrestling moves and techniques: typical wrestling skills such as takedowns, escapes, bridges, pin combinations, and so on (20 minutes);
- muscular endurance and anaerobic capacity: a combination of bodyweight exercises such as pull-ups, push-ups, dips and rope climbing and weightlifting (30 minutes);
- partner exercises: wrestling with a partner of similar bodyweight in full-speed 6-minute matches (10 minutes).

### Laboratory analysis

Blood was drawn into serum tubes before and immediately after the exercise training session. The blood samples were shipped to the Biochemical Laboratory of the Medical University of Kocaeli for biochemical measurements of IMA and serum albumin. The blood samples were transferred to plain tubes containing no preservatives. Clot formation was allowed for 30 minutes and the blood samples were centrifuged before separating the serum. Then, the obtained serum samples were subjected to measurement immediately. ACB was analyzed according to the method described by Bar-Or et al. (2000). In this method, 200  $\mu$ L of serum is added to the water solution of 50  $\mu$ L 0.1% (w/v) cobalt chloride ( $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ ; Sigma-Aldrich Inc., St Louis, MO, USA). It was mixed gently and left to sit for 10 minutes to allow for sufficient cobalt-albumin binding to occur. Then, 50  $\mu$ L of dithiothreitol ( $1.5 \text{ mg} \cdot \text{mL}^{-1} \text{ H}_2\text{O}$ ; Sigma-Aldrich Inc.) was added as a colorizing agent. After waiting for 2 minutes, 1.0 mL of 0.9% NaCl was added to stop the cobalt-albumin binding process. Next,

**Table 1.** Subject characteristics ( $n = 20$ )\*

Age (yr)	$28.8 \pm 8.96$
Height (cm)	$175.55 \pm 7.23$
Weight (kg)	$80.95 \pm 15.99$
BMI [ $\text{kg} \cdot (\text{m}^2)^{-1}$ ]	$26.15 \pm 3.69$

\*Data presented as mean  $\pm$  standard deviation. BMI = body mass index.

absorbance was measured using a spectrophotometer (model UV160U; Shimadzu Corp., Kyoto, Japan) at 470 nm. Blank sample without dithiothreitol was used as blind. The results were reported in absorbance units (ABSU). This colorimetric method of measurement scanning is based on the principle of quantitative scanning for free cobalt present after cobalt binding has taken place. This means that high absorbance levels as a result of increased amounts of free cobalt in the environment can be determined (Mentese et al. 2008). In our laboratory, the mean within-run percent coefficient of variation for the IMA assay is 3.0%.

Serum albumin concentrations were studied using an automated analytical chemistry system (Modular Analytics; Roche Diagnostics, Mannheim, Germany), based on a colorimetric bromocresol green method. The reagent was used according to the manufacturer's instructions and the analytical performance was within the manufacturer's specifications.

Blood lactate levels were analyzed using the Accutrend Lactate Analyzer (Roche Accusport; Roche Diagnostics). The analyzer was calibrated using the standard control solutions prior to each testing session. Lactate values were determined at rest and after exercise. Blood samples were drawn from the athletes' fingertips using a disposable surgicut device. Because of the close association of IMA with serum levels of lactate and albumin (Falkensammer et al. 2007), we evaluated IMA values together with these parameters.

### Statistical analysis

After tests for normality, the nonparametric Mann-Whitney *U* test was used to test differences between pre-exercise and post-exercise data. Means  $\pm$  standard deviations are given as descriptive statistics. The relationship between IMA, albumin and lactate levels was evaluated by correlation analysis. Pearson's correlation

test was used to assess the correlation between variables. SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. A *p* value  $< 0.05$  was considered to be statistically significant.

Receiver operating characteristic (ROC) curve analysis was performed to determine the specificity and sensitivity of the cutoff values for all the wrestlers (MedCalc version 9.4.2; MedCalc Software, Mariakerke, Belgium). The area under the curve was calculated with its standard error and 95% confidence interval (CI).

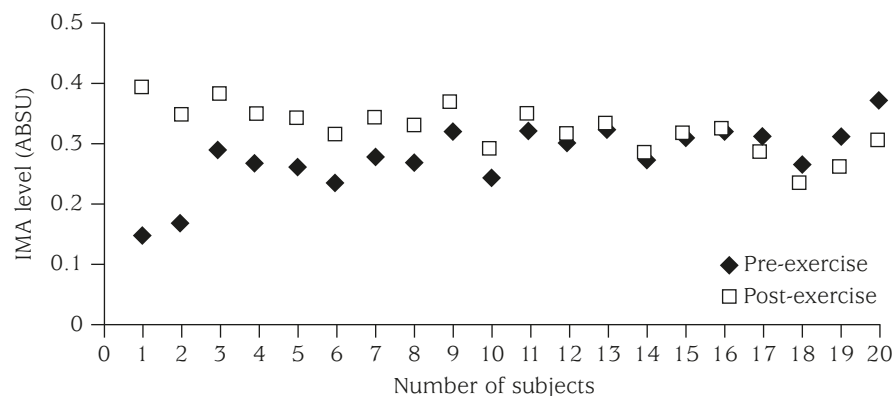
### Results

Results of the biochemical measurements are shown in Table 2. Mean serum IMA levels were  $0.281 \pm 0.052$  ABSU before exercise and  $0.324 \pm 0.039$  ABSU after exercise ( $p < 0.05$ ; Figure 1). This difference was statistically significant ( $p < 0.005$ ; 95% CI, 0.03–1.40). For wrestlers' ROC curve analysis, the area under the curve for IMA was 0.765 (95% CI, 0.604–0.884; Figure 2). Exploratory analysis of different cutoff points was performed with the ROC curve (Table 3). In our study, on the basis of the ROC curve, with a cutoff point of 0.170 ABSU for the determination of ischemia, the IMA assay was 100% sensitive but demonstrated a low specificity of 10%. At a cutoff point of 0.263 ABSU, the IMA assay was highly sensitive but specificity remained low. The IMA

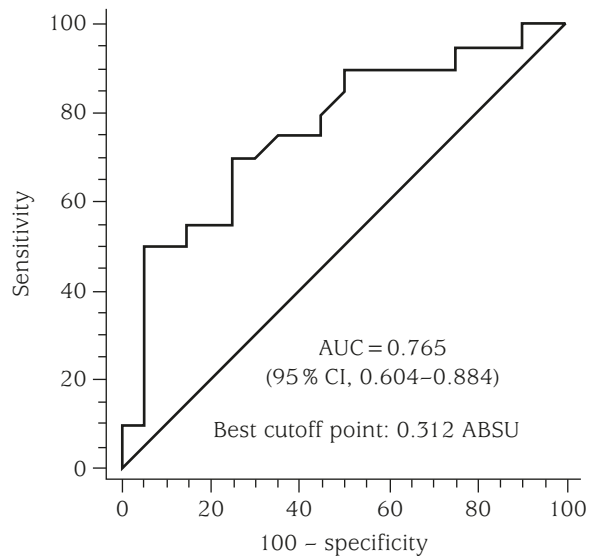
**Table 2.** Pre- and post-exercise ischemia-modified albumin (IMA), albumin and lactate\*

	Pre-exercise	Post-exercise	<i>p</i>
IMA (ABSU)	$0.281 \pm 0.052$	$0.324 \pm 0.039$	0.004
Albumin ( $\text{g} \cdot \text{dL}^{-1}$ )	$4.70 \pm 0.17$	$4.96 \pm 0.15$	0.000
Lactate ( $\text{mmol} \cdot \text{L}^{-1}$ )	$1.70 \pm 0.66$	$4.38 \pm 0.85$	$< 0.001$

\*Data presented as mean  $\pm$  standard deviation.



**Fig. 1** Changes in ischemia-modified albumin (IMA) levels from before to after exercise.



**Fig. 2** Receiver operating characteristic curve analysis for the ischemia-modified albumin assay. AUC = area under the curve; CI = confidence interval.

**Table 3.** Sensitivity and specificity of the albumin-cobalt binding assay for ischemia-modified albumin (IMA) across various cutoff points\*

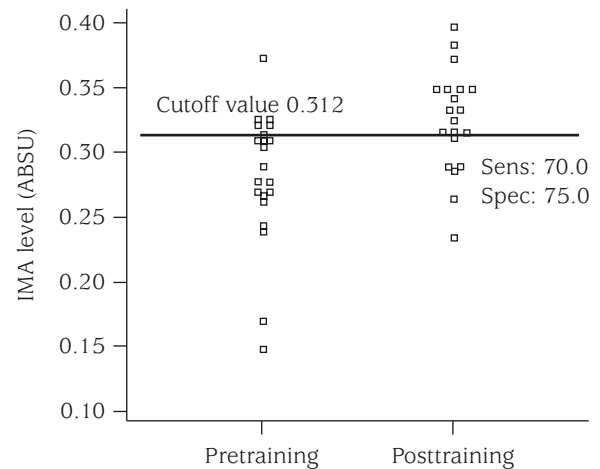
IMA (ABSU)	Sensitivity (%)	Specificity (%)
0.170	100	10
0.263	95	25
0.312	70	75

\*95% confidence interval = 0.768-0.933.

value with the most acceptable sensitivity and specificity was 0.312 ABSU (sensitivity of 70%, specificity of 75%; Figure 3). This value, with satisfactory sensitivity and specificity, was regarded as a suitable cutoff point. However, if IMA is to be assessed as a potential diagnostic test, a sensitivity of 70% and a specificity of 75% are clearly unacceptable.

Surprisingly, 5 out of 20 subjects exhibited low IMA concentrations (less than the cutoff value) after exercise. In fact, neither the athletic features nor the exercise regimens of these subjects were different from those of the other athletes. Even if we had excluded these subjects, the IMA levels would still have been significantly higher in the wrestlers than in the controls.

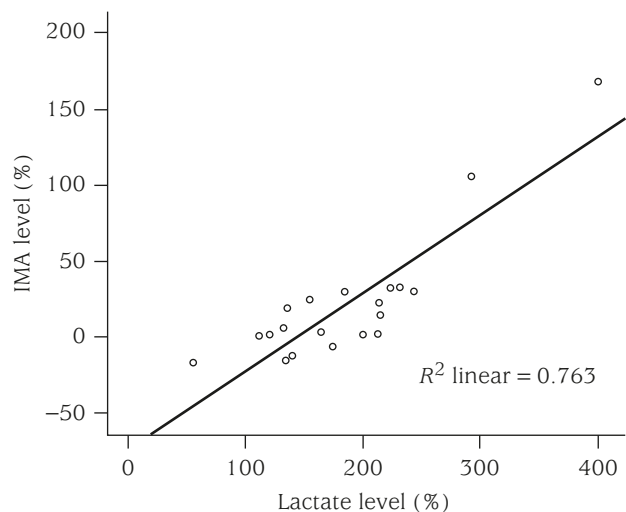
After exercise, mean serum albumin levels were significantly increased ( $4.96 \pm 0.15 \text{ g} \cdot \text{dL}^{-1}$ ) compared to before exercise ( $4.70 \pm 0.17 \text{ g} \cdot \text{dL}^{-1}$ ;  $p < 0.05$ ). At rest, mean blood lactate level was  $1.70 \pm 0.66 \text{ mmol} \cdot \text{L}^{-1}$ , compared to  $4.38 \pm 0.85 \text{ mmol} \cdot \text{L}^{-1}$  5 minutes after training ( $p < 0.05$ ).



**Fig. 3** Scattergram of ischemia-modified albumin (IMA) levels in wrestlers before and after exercise.

**Table 4.** Post-exercise correlation between changes in ischemia-modified albumin (IMA), albumin and lactate

	<i>p</i>	<i>r</i>
IMA-lactate	< 0.001	0.873
Albumin-lactate	0.613	-0.120
IMA-albumin	0.807	-0.058



**Fig. 4** Correlation between ischemia-modified albumin (IMA) and lactate.

The results of the correlation tests between IMA, lactate and albumin levels are shown in Table 4. A significant positive correlation ( $r = 0.873$ ;  $p < 0.001$ ) was found between IMA and lactate levels (Figure 4), but not between IMA and albumin ( $r = -0.058$ ;  $p = 0.807$ ) and between albumin and lactate ( $r = -0.120$ ;  $p = 0.613$ ).

## Discussion

We examined whether or not plasma IMA levels change after intense exercise in wrestlers. Many studies show that skeletal muscle ischemia can result in changes in IMA levels. Recent reports have shown conflicting results with regard to the effects of exercise on serum IMA concentrations. Many studies suggest that exercise is associated with decreased IMA levels (Middleton et al. 2006; Roy et al. 2004; Zapico-Muniz et al. 2004). Apple et al. (2002) demonstrated an immediate reduction in IMA following completion of a marathon, which was followed by an increase in IMA 24–48 hours after exercise. Some authors have suggested that the immediate decrease in IMA concentration after physical exercise may be attributable to interference with IMA measurement by the lactate produced during skeletal muscle ischemia (Zapico-Muniz et al. 2004; Apple et al. 2002). In contrast, there have also been reports of immediate elevation in IMA levels following exercise. A recent investigation demonstrated that exercise-induced calf muscle ischemia resulted in a short period of IMA elevation in a group of healthy volunteers (Falkensammer et al. 2007). In a study by Lippi et al. (2005), the concentration of IMA was significantly increased in athletes subjected to high-workload endurance training. After all, it is questionable whether aerobic and anaerobic exercise bouts have differing effects on serum IMA levels. We found that serum IMA levels increased significantly after exercise. Indeed, compared with other athletes, the anaerobic performance of wrestlers is more similar to that of power athletes than endurance athletes on the basis of equivalent bodyweight (Yoon 2002). It is possible that, owing to the high-intensity workload applied in this study, we observed significant increases in this marker. Such an increase was, however, present only in some athletes who were subjected to high-workload exercise (Lippi et al. 2005).

Intense anaerobic exercise often damages skeletal muscle (Ihara et al. 2001). Tissue damage usually leads to increased reactive oxygen/nitrogen species formation and oxidative stress. The effects of anaerobic exercise on oxidative stress have been studied and reviewed previously. It has been shown that acute anaerobic exercise serves as a sufficient stimulus to elicit an increase in reactive oxygen/nitrogen species formation (Fisher-Wellman & Bloomer 2009; Bailey et al. 2004), and collectively, it appears that all forms of anaerobic exercise possess the ability to result in increased oxidative stress, evident by several studies reporting an increase in oxidative stress biomarkers following exercise

(Bloomer et al. 2005). IMA appears to be an indicator of oxidative stress (Collinson & Gaze 2008). It has been proposed that albumin modification by reactive oxygen species produced during ischemia leads to IMA formation. The generation of reactive oxygen species can at least transiently modify the N-terminal region of albumin to yield increased levels of IMA (Roy et al. 2004). It may be possible that an increase in oxidative stress during anaerobic activity might result in an elevation of IMA levels in this study.

Blood lactate concentration in wrestlers has recently been used as an indicator of anaerobic power and capacity in successful wrestlers (Yoon 2002). Successful wrestlers may be more tolerant of lactate (lactate tolerance) as well as more capable of blood buffering for muscular endurance (Aschenbach et al. 2000). A few authors have found significant elevations in lactate concentrations either after wrestling matches (Kraemer et al. 2001) or after exercise (Hubner-Woźniak et al. 2004), showing the anaerobic nature of wrestling. The generally agreed-on lactate value for the transition of aerobic to anaerobic exercise is  $>4 \text{ mmol} \cdot \text{L}^{-1}$ . The mean lactate concentration found in the present study was  $4.38 \text{ mmol} \cdot \text{L}^{-1}$ . The concentrations of lactate that we found in wrestlers indicated that wrestling exercise led to an anaerobic state. Zapico-Muniz et al. (2004) reported elevated lactic acid levels that accompanied IMA decrease following ischemic exercise; however, the cause of this was not explained. The authors suggested interference of the ACB test by lactate.

We found no association of IMA levels with albumin. Negative correlation between IMA and serum albumin has been described previously (Falkensammer et al. 2007; Zapico-Muniz et al. 2004). Total albumin is known to rise in response to prolonged exercise as it is essential in the mobilization of free fatty acids (Convertino et al. 1980), a preferred fuel source during prolonged exercise (Shave et al. 2007). In the present study, prolonged strenuous anaerobic exercise may result in higher serum albumin levels. Albumin concentration changes that occur after strenuous exercise need to be more fully understood.

Another factor responsible for the increase in IMA may be exercise-induced cardiac damage. Prolonged endurance exercise has been associated with left ventricular wall motion abnormalities (La Gerche et al. 2008; Kasikcioglu et al. 2005), anomalies in cardiac structure or function, as well as cardiac biomarker changes (Neilan et al. 2006). Although IMA has been used as a marker of myocardial ischemia, little is known about its production during ischemia of other tissues (Troxler

et al. 2006). Troxler et al. concluded that when IMA is used to detect myocardial ischemia, ischemic skeletal muscle must be excluded. Unfortunately, other cardiac biomarkers such as cardiac troponin T could not be measured in our athletes, which is a limitation of the study. Therefore, our results could not be attributed to exercise-induced cardiac ischemia.

Our study shows that IMA, which is a biomarker of ischemia, is likely to increase as a result of intense anaerobic exercise. However, further studies are required to examine the relationship between anaerobic exercise and tissue ischemia.

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