

Muscle Damage, Soreness, and Stress Over 7-weeks of Pre-season Training In NCAA D1

Female Swimmers

Submitted By

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### Abstract

In 2014, three female swimmers were hospitalized with symptomatic exertional rhabdomyolysis (Stanfa et al., 2016). **PURPOSE:** To serially monitor and assess relationships between skeletal muscle damage, upper and lower body soreness, and physiological stress during the first seven weeks of high volume training in collegiate female swimmers. **METHODS:** 23 female NCAA D1 swimmers presented to the lab six times during 7-weeks of pre-season training. Blood was drawn at six timepoints for measurement of serum creatinine kinase (CK), myoglobin (MYO) and a complete metabolic panel. Serum cortisol (C), testosterone (T) and T/C ratio were assessed at Weeks 1 (baseline), 4 and 7. Upper body soreness (US) and lower body soreness (LS) were assessed, at the six timepoints that blood was drawn, using a visual analogue scale (0-10-inch unmarked scale). A repeated measures ANOVA with a Bonferroni correction were performed, with data reported as means±SD. Correlation analyses performed with significance set at  $p<0.05$ . **RESULTS:** Weekly training load consisted of: 88% swimming, 6% running, and 6% weight training which gradually increased from 16 hours to 20 total training hours/week over the first seven weeks of training. Significant changes were noted in CK (135±68; 446±723; 171±83; 202±80; 180±100; 206±170;  $p=0.01$ ), US (1.5±1.8; 3.9±1.7; 3.3±1.8; 5.4±1.6; 6.1±1.8; 3.7±2.0;  $p<0.0001$ ), LS (1.3±1.5; 5.0±2.2; 3.4±1.8; 5.0±1.9; 4.8±1.8; 4.1±2.0;  $p<0.0001$ ), cortisol (19±10; 15±6; 11±5ng/dL;  $p<0.0001$ ), and T/C ratio (2.4±2.3; 3.0±1.8; 4.1±2.8;  $p=0.0003$ ) but not in MYO (39±20; 63±141; 29±18; 30±17; 24±4ng/mL; 29±14ng/mL;  $p=0.32$ ) or testosterone (33±14; 37±14; 36±14 ng/dL;  $p=0.29$ ). Significant correlations noted between CK vs. MYO ( $r=0.84$ ), alanine aminotransferase ( $r=0.21$ ), and aspartate aminotransferase ( $r=0.49$ ) when data were combined, but largely driven by an outlier with CK=3558 ng/mL and MYO=691ng/mL at

Week 2 (first training week). CONCLUSION: Muscle damage in collegiate female swimmers remained largely within the normal range (CK<200U/L) on average, but was highly variable between individuals. No correlations noted between muscle damage (CK, MYO) and (upper and lower) body soreness, at moderate (2-6) ratings of muscle soreness. Serum cortisol declined over training, promoting an anabolic hormonal environment.

### Introduction

Rhabdomyolysis is a syndrome that results from injury to skeletal muscle that alters the integrity of the cell membrane, resulting in subsequent breakdown of muscle fibers and leakage of those contents into extracellular fluid. Most notable of these muscle fibers include creatine kinase (CK), myoglobin, and electrolytes (Gabow et al., 1982, Galvez et al., 2008). Serum CK levels five times higher than normal value typically confirms rhabdomyolysis, and though there is no current accepted hospitalization level, CK greater than ten times the upper limit (approximately  $2000 \text{ U} \cdot \text{L}^{-1}$ ) is frequently used as a marker (Clarkson et al., 2006, Lima et al., 2008). Symptomatic rhabdomyolysis is often denoted by a classic triad of symptoms which includes muscle pain, weakness, and dark urine (Cervellin et al., 2010, Galvez et al., 2008). However this can be misleading, as <10% of patients show this triad, and >50% demonstrate asymptomatic rhabdomyolysis and do not experience muscle weakness at all (Torres et al., 2015).

The main causes of rhabdomyolysis include direct muscular injury, strenuous exercise, drugs, alcoholism, infections, hyperthermia, seizures, hypothermia (Gabow et al., 1982). Acute kidney injury is the most serious complication associated with rhabdomyolysis, which is the result of an accumulation of myoglobin, a nephrotoxic substance, in the kidney (Torres et al., 2015). Rhabdomyolysis accounts for 7-10% of acute kidney injury cases in the United states, and of those diagnosed with rhabdomyolysis, 33-50% of patients experience acute kidney injury (Bosch et al., 2009, Lima et al., 2008).

Acute kidney injury occurs when there is volume depletion due to the sequestration of water in injured muscles, (Bosch et al., 2009). To compensate for this loss, aggressive forced

hydration is required using sterile saline and glucose solutions (Cervellin et al., 2010). This intravenous resuscitation replaces fluid into the intravascular space that may have been sequestered in large amounts into areas of myocyte damage and it increases urine flow to the tubules to prevent renal failure from myoglobin deposition (Galvez et al., 2008). Plainly, it clears out the toxins that have made it into the bloodstream and flushes the body of waste. The goal of volume expansion is to maintain urine output at more than 200-300 ml/hour (Bosch et al., 2009, Cervellin et al., 2010, Lima et al., 2008, Smoot et al., 2013). It is also important to maintain urine pH levels between 6.5-7.5, which can be done by adding sodium bicarbonate to the intravenous regimen (Cervellin et al., 2010, Torres et al., 2015).

Exertional rhabdomyolysis (ER) is characterized by exercise-induced muscle fiber breakdown. There is a great amount of literature surrounding ER in endurance events such as triathlons and marathons, weight lifting, and military basic training (Galvez et al., 2008). Several risk factors such as inadequate hydration, high ambient temperature, and supplement use are associated with the development of this syndrome (Furman, 2015). Physically untrained individuals are typically those found with exertional rhabdomyolysis, but conditioned athletes who unexpectedly increase the volume and intensity of their workouts have also been found to be susceptible (Smoot, et al.). This is why many describe ER as “too much, too fast, too soon” of any particular exercise (Eichner, 2011).

Eccentric contractions have been found to be a common theme in athletes who exhibit ER. In one study, 100 back squats were completed using different time intervals and number of sets, CK levels ranging from 96,987 to 331,044 U/L (Smoot et al., 2013). A different case study following another collegiate football player performed 10 sets of 30 repetition squatting

exercises (300 total) was found to have 130,899 U/L at time of admittance to the hospital (Moeckel-Cole & Clarkson, 2009). Eccentric muscular contractions found in exercises such as running downhill during marathons, ultra marathons, and triathlon races have also been seen to increase these levels (bruso et al., 2010; Noakes, 1987; Souza et al., 2006).

Exertional rhabdomyolysis has become more prevalent in Division 1 sports today. Five clusters of symptomatic exertional rhabdomyolysis have been reported in National Collegiate Athletic Association (NCAA) athletes, of which including football, lacrosse, and swimming (Stanfa et al., 2016). In sports such as these, it is often found that clusters occur during a time directly following a break or during pre-season training in their sport (Eichner, 2013; Galvez et al., 2008; Stanfa et al., 2016; Smoot et al., 2013).

In 2008, a case report surrounding seven division-1 swimming athletes was published. This was the first case of ER to be reported in recent literature and entailed 3 consecutive days of upper-extremity dry-land training (Galvez et al., 2008). In 2016, a second case report of rhabdomyolysis was published in collegiate swimmers. This case cluster involved well-trained, in-shape, athletes who underwent a dry land, short interval, high intensity, upper-extremity competition (Stanfa et al., 2016). Though renal failure is a potentially serious complication associated with rhabdomyolysis, these case studies both suggested that upper-extremity workouts that cause high levels of CK typically do not lead to renal failure. However, there is no algorithm that has the ability to predict when detrimental effects such as renal failure might occur (Galvez et al., 2008).

The female swimmers that were hospitalized in the study by Stanfa et al also showed signs of overtraining marked by elevated blood pressure and decreased lean mass over 16 weeks

of training (Stanfa et al 2016). Other studies have looked at overtraining syndrome by evaluating the ratio between the hormones, cortisol and testosterone. In response to the acute stress of physical activity, both cortisol and testosterone are released into the bloodstream and are catabolic and anabolic, respectively (Emami et al., 2016). In other words, cortisol tears down muscle mass while testosterone stimulates skeletal muscle growth. This catabolic/anabolic relationship is essential to initiate an increase in muscle growth (Tanner et al., 2014). Sometimes, the testosterone/cortisol ratio is used to assess the relationship between the building muscle/breaking down muscle, with the higher the value the more muscle breakdown that is occurring (Emami et al., 2016). A higher testosterone/cortisol ratio would be indicative of overtraining (and over-reaching, which can lead to overtraining).

The primary purpose of this study was to serially track the trajectories and evaluate the relationships between muscle damage, muscle soreness, and over-reaching in female collegiate swimmers during the first six weeks of pre-season training. We hypothesize that the markers of muscle damage (creatinine kinase, myoglobin, alanine transaminase, aspartate transaminase) will correlate with muscle soreness (upper and lower body), which would peak after the first week of training. We also hypothesize that cortisol (the hormone of stress) will increase while testosterone (the muscle-building hormone) will decrease over time and training, leading to a temporary over-reaching syndrome in response to heavy training.

## Methods

### Participants

After obtaining approval from Oakland University's Institutional Review Board, 23 female collegiate swimmers were recruited on a voluntary basis with informed consent. All of the participating swimmers were healthy, with an age range between 17-21 years.

### Materials and Procedures

All participants were tested a total of six times. For the female swimmers, this study took place over a seven-week period. The first data collection happened after informed consent forms were signed and before the first day of official practice at Oakland University. The first data collection was used to determine baseline values for each of the key outcome variables described below. For the next six weeks after the first data collection, all swimmers reported to the Prevention Research Center weekly, at 4pm on Friday afternoons. During these testing sessions, the following measurements were obtained:

Height and weight were measured using a balance scale with stadiometer. Seated blood pressure was also measured at the beginning of every trial, for a separate project.

#### Blood sampling

Per session, 10mL (2 teaspoons) of blood were collected via venipuncture by trained medical professional. All serum samples were analyzed at the Crittenton Hospital Laboratory for measurement of: albumin (ALB), alkaline phosphatase (ALK), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatine kinase (CK), carbon



dioxide (CO<sub>2</sub>), creatinine, glucose (GLU), total protein (TP), calcium (CA<sup>++</sup>), total bilirubin (BIL), sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), Chloride (Cl<sup>-</sup>), anion gap (AG), and myoglobin (MYO). Blood samples were also analyzed for cortisol (C) and testosterone (T) on weeks 1 (baseline), 4 (mid-testing), and 7 (final testing). *For this thesis, the main outcome variables that we will analyze include: creatine kinase (CK), myoglobin (MYO), alanine aminotransferase (ALT), aspartate aminotransferase (AST), testosterone, and cortisol.* Together, these blood tests assess muscle damage as well as training stress. The other blood markers will be analyzed outside of this thesis.

#### Urine sampling

Per session, participants were asked to provide a urine sample by urinating in a small plastic cup. Each urine sample was analyzed using a URS-10 CHEMSTRIP inserted into a Uritek TC-101 urine reader (Teco Diagnostics, Anaheim, CA) for measurement of: glucose [GLU], bilirubin [BIL], ketones [KET], specific gravity [USG], blood [BLD], pH, proteins [PRO], nitrogen [NIT].

#### Body Composition measurement using the BodPod

Body composition was measured using air displacement plethysmography via a “BodPod” device on the first (session 1; baseline) and last (session 6; final) day of testing. The BodPod estimates the amount of fat and lean mass by measuring the amount of air that is displaced around the body while sitting quietly in this egg-shaped chamber. Here is a picture of the BodPod:



### Muscle soreness scale

Participants were given a soreness scale every session. The soreness scale consisted of a 10-inch (25.4cm) visual analogue scale (VAS), asking participants to mark how sore they were on a horizontal, scoreless straight line representing “no soreness at all” on the left start of the line to “maximum amount of muscle soreness” on the right end of the line. Participants were asked to rate both *upper body soreness* (US) and *lower body soreness* (LS) in real-time. This would represent any feelings of soreness at that moment. The horizontal distance from the left anchor of the line (no soreness) to the participant’s “mark” of soreness was then measured using the 10-inch ruler. This measured distance in inches corresponded with the amount of “soreness” on a scale from 0-10.

### **Statistical Analyses**

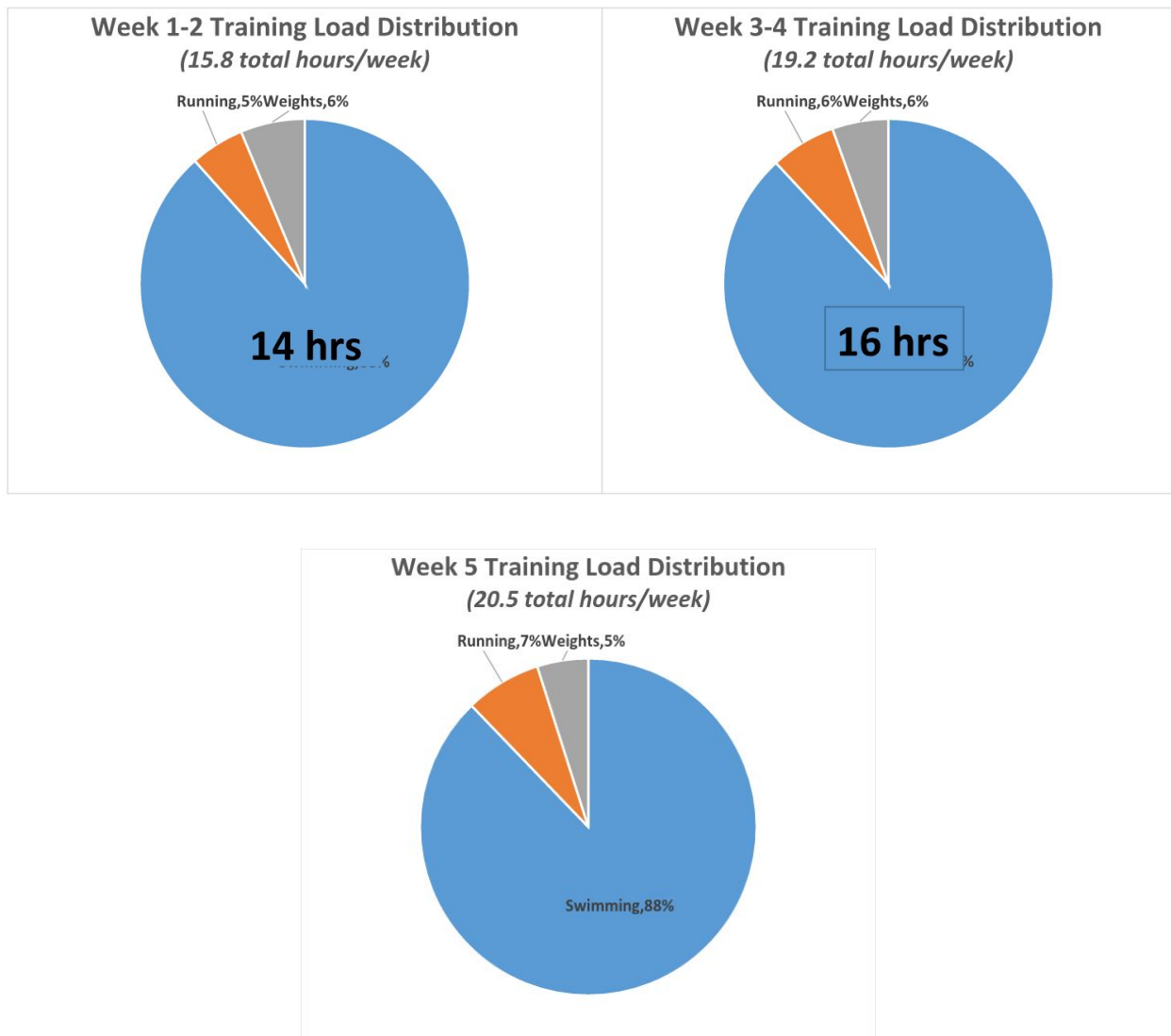
All data were analyzed using the STATISTICA version 14 software (Stat Soft, Tulsa, OK, USA). Repeated measures ANOVA with a Bonferroni correction were performed for all outcome measures. The main outcome measure was serum CK. All data were reported as means  $\pm$  standard deviation (SD), with statistical significance set *a priori* at  $p < 0.05$ .

## **Results**

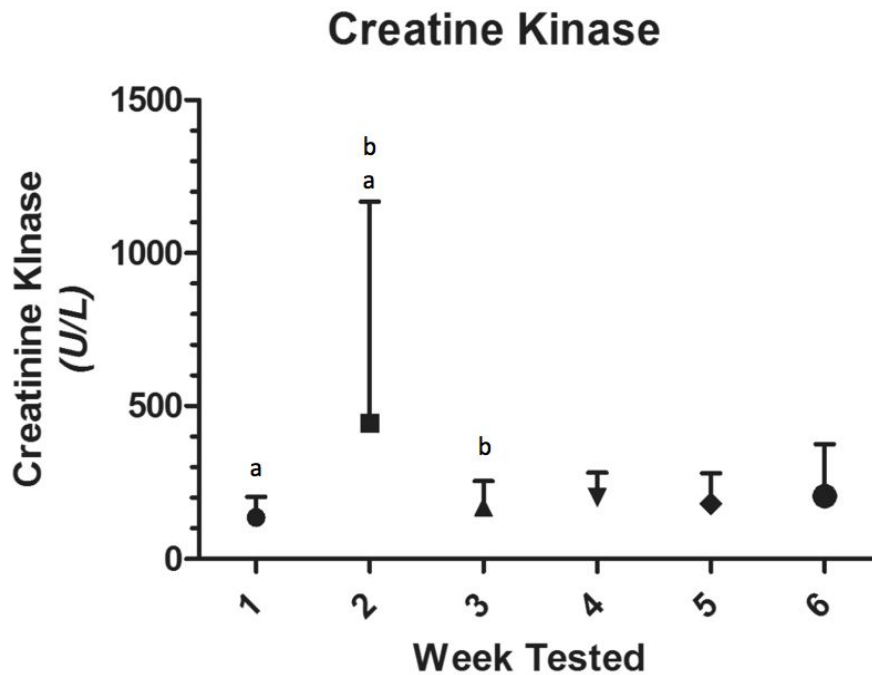
Twenty-three healthy female collegiate athletes ranging in ages from 17-21 participated in the study. Weekly training load consisted of: 88% swimming, 6% running, and 6% weight training which gradually increased from 16 hours to 20 total training hours/week over the first seven weeks of training (Figure 1). Significant changes were noted in CK ( $135 \pm 68$ ;  $446 \pm 723$ ;  $171 \pm 83$ ;  $202 \pm 80$ ;  $180 \pm 100$ ;  $206 \pm 170$ ;  $p = 0.01$ ), US ( $1.5 \pm 1.8$ ;  $3.9 \pm 1.7$ ;  $3.3 \pm 1.8$ ;  $5.4 \pm 1.6$ ;  $6.1 \pm 1.8$ ;

3.7±2.0; p<0.0001), LS (1.3±1.5; 5.0±2.2; 3.4±1.8; 5.0±1.9; 4.8±1.8; 4.1±2.0; p<0.0001), cortisol (19±10; 15±6; 11±5ng/dL; p<0.0001), and T/C ratio (2.4±2.3; 3.0±1.8; 4.1±2.8; p=0.0003) but not in MYO (39±20; 63±141; 29±18; 30±17; 24±4ng/mL; 29±14ng/mL; p=0.32) or testosterone (33±14; 37±14; 36±14ng/dL; p=0.29). Significant correlations noted between CK vs. MYO (r=0.84), alanine aminotransferase (r=0.21), and aspartate aminotransferase (r=0.49) when data were combined, but largely driven by an outlier with CK=3558ng/mL and MYO=691ng/mL at Week 2 (first training week).

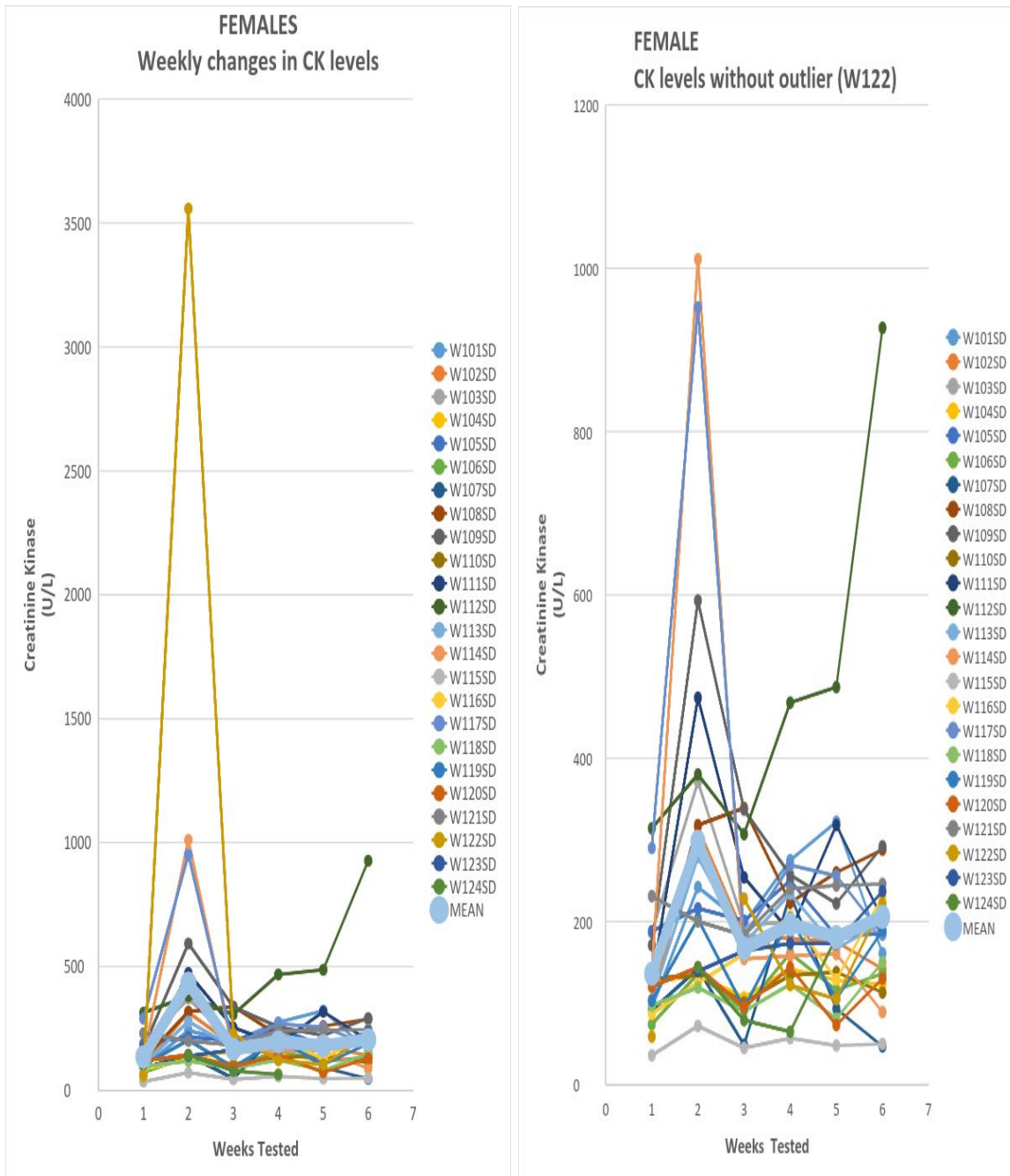
**Figure 1:** Training load over the first six weeks of pre-season training



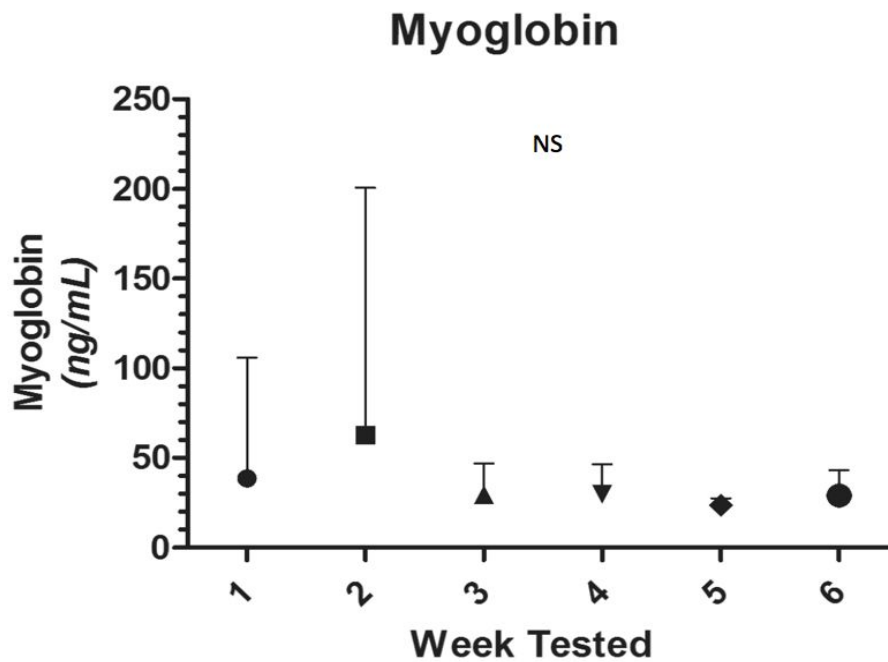
**Figure 2a:** Repeated-measures ANOVA for serum creatine kinase concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean serum creatinine kinase levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. a,b) =  $p < 0.05$ .



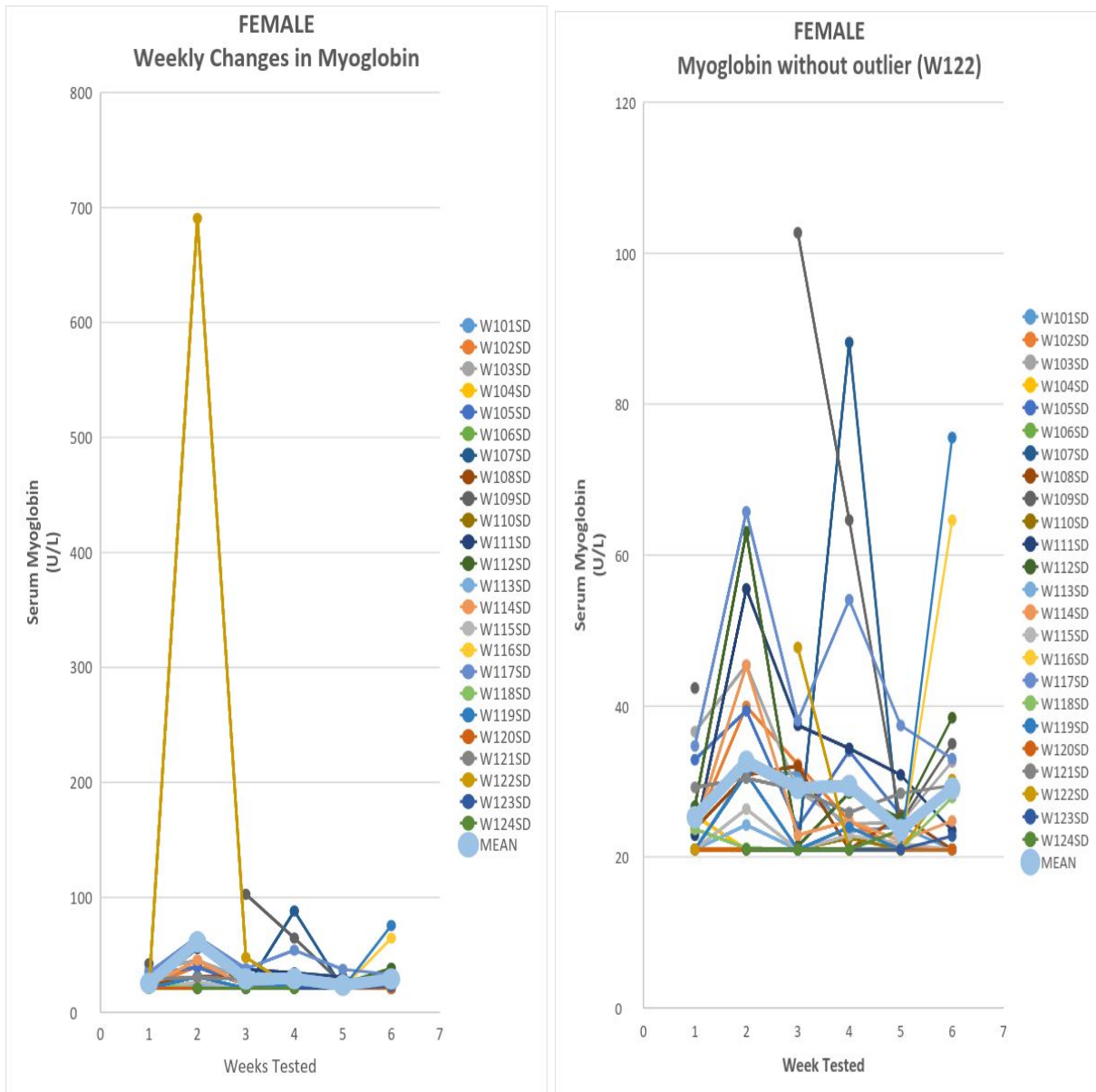
**Figure 2b:** Individual trajectories for serum creatinine kinase concentrations are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line. There was one outlier, so the graph on the left includes everyone while the graph on the right is without the outlier.



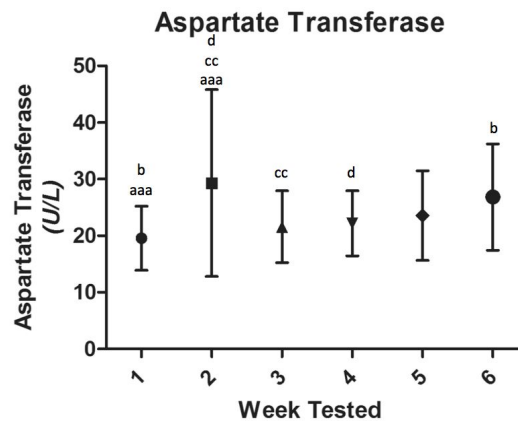
**Figure 3a:** Repeated-measures ANOVA for serum myoglobin concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. a,b) =  $p < 0.05$ .



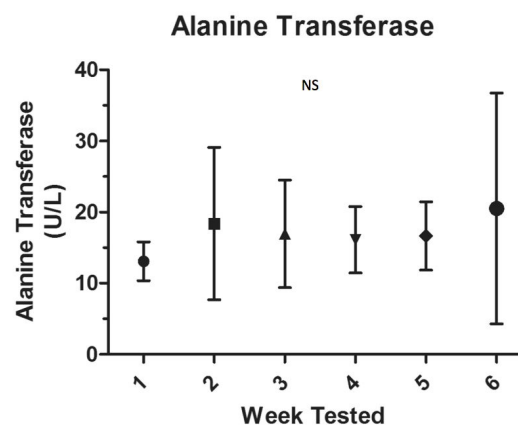
**Figure 3b:** Individual trajectories for serum myoglobin concentrations are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line. There was one outlier, so the graph on the left includes everyone while the graph on the right is without the outlier.



**Figure 4:** Repeated-measures ANOVA for serum aspartate transferase concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean serum creatinine kinase levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. b,d) =  $p < 0.05$ ; double letters (i.e. cc) =  $p < 0.01$ ; triple letters (i.e. aaa) =  $p < 0.001$ .

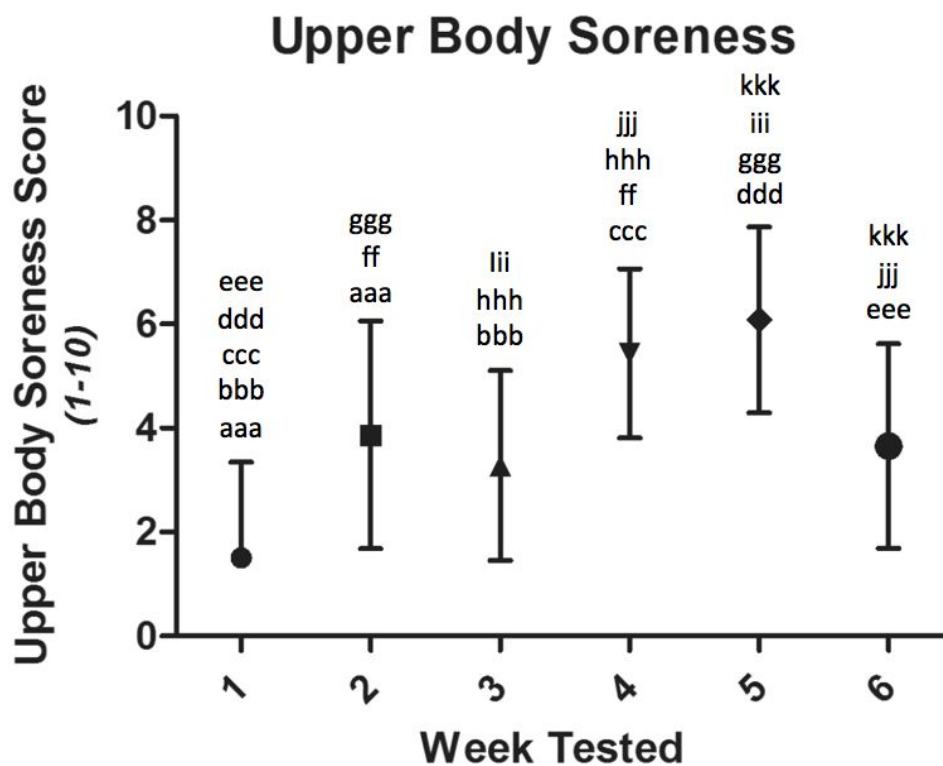


**Figure 5:** Repeated-measures ANOVA for serum alanine transferase concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Results non-significant (NS).

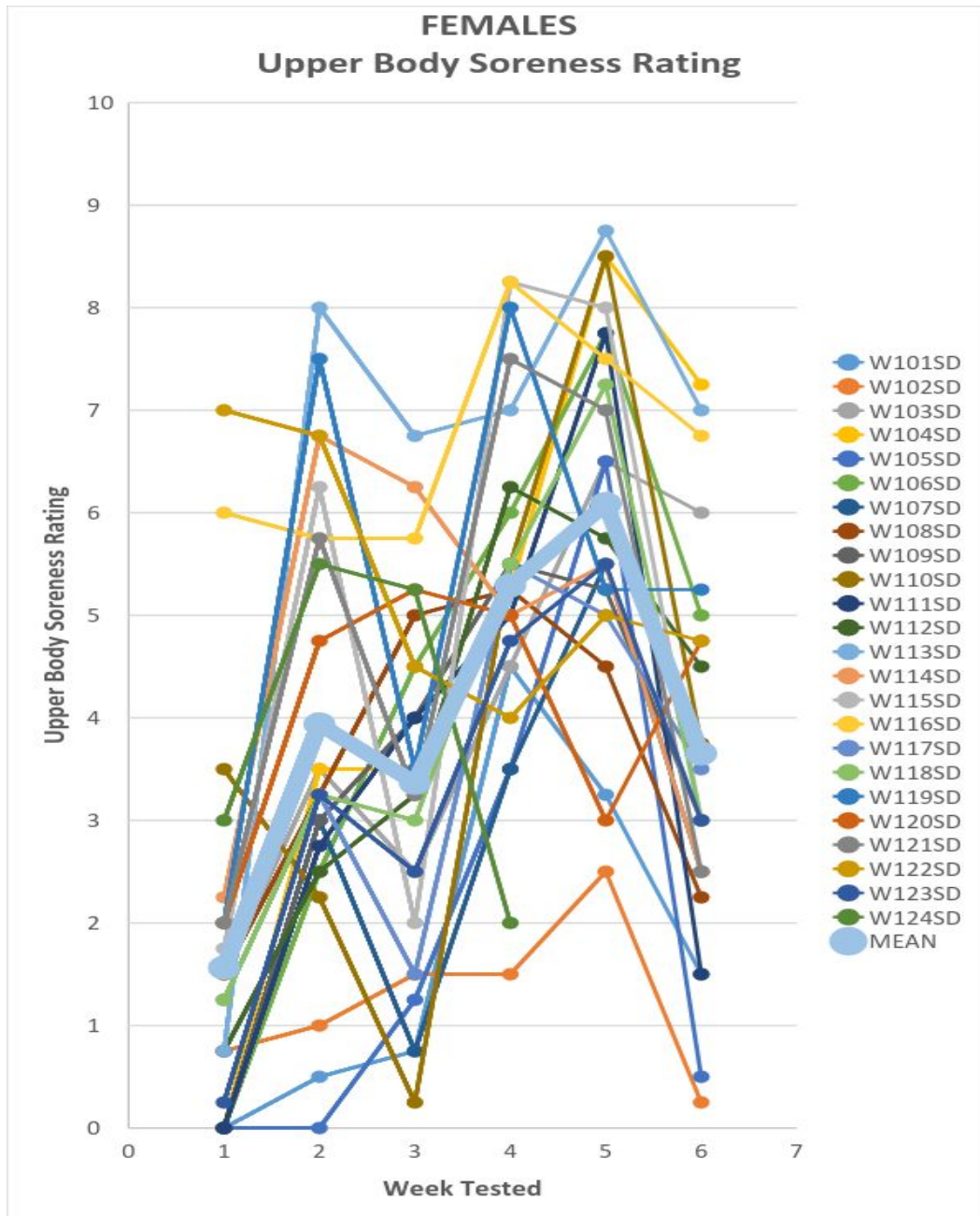




**Figure 6a:** Repeated-measures ANOVA for upper body soreness. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: double letters (i.e. ff) =  $p < 0.01$ ; triple letters (i.e. aaa, bbb, ccc, ddd, eee, ggg, hhh, iii, kkk) =  $p < 0.001$ .



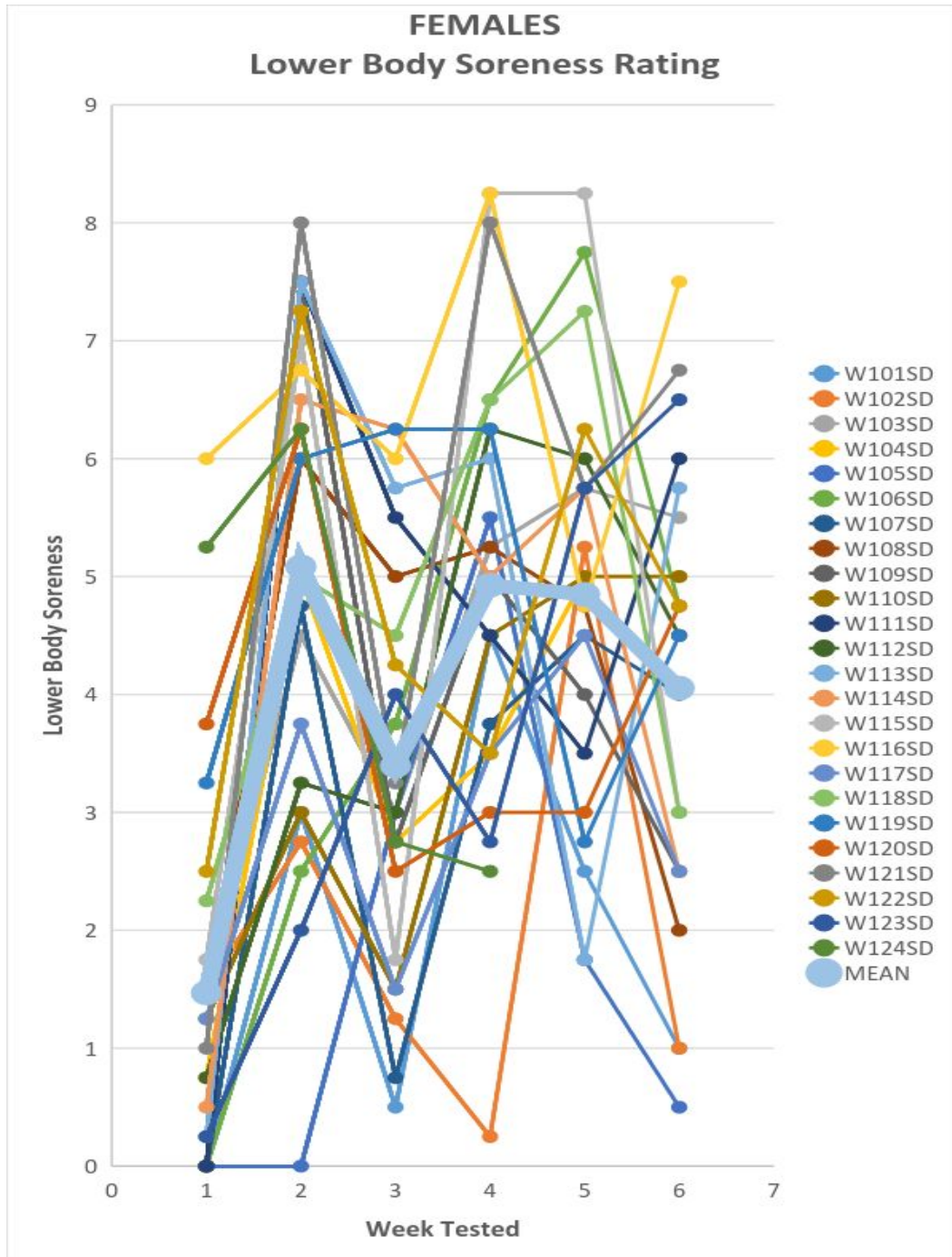
**Figure 6b:** Individual trajectories for upper body soreness are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line.



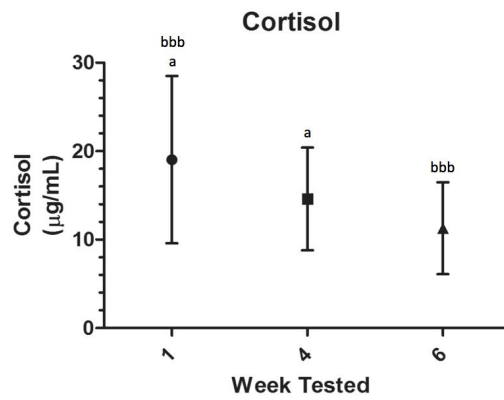
**Figure 7a:** Repeated-measures ANOVA for lower body soreness. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. f, g, h) =  $p < 0.05$ ; triple letters (i.e. aaa, bbb, ccc, ddd, eee) =  $p < 0.001$ .



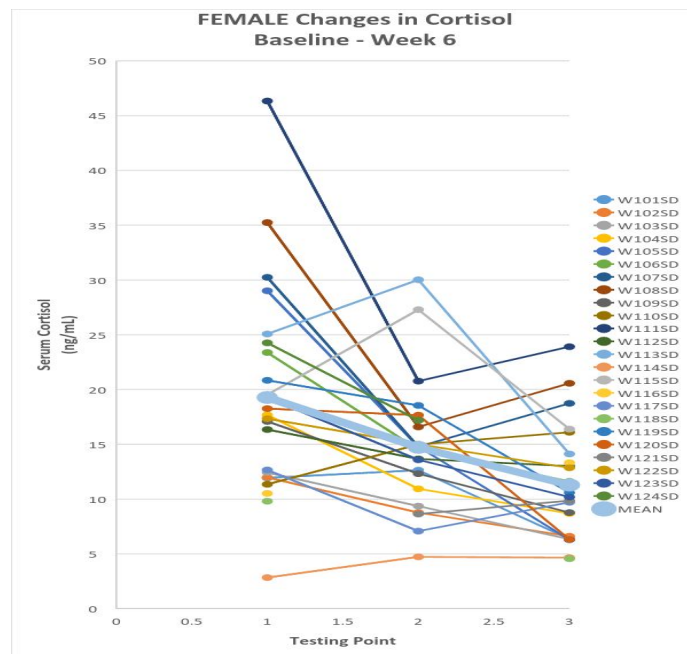
**Figure 7b:** Individual trajectories for lower body soreness are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line.



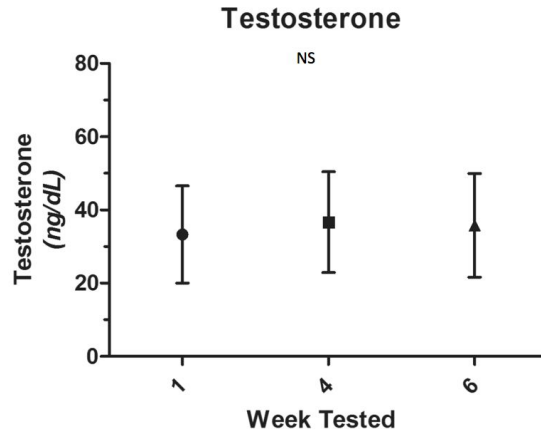
**Figure 8a:** Repeated-measures ANOVA for serum cortisol concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean serum levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. a) =  $p < 0.05$ ; triple letters (i.e. bbb) =  $p < 0.001$ .



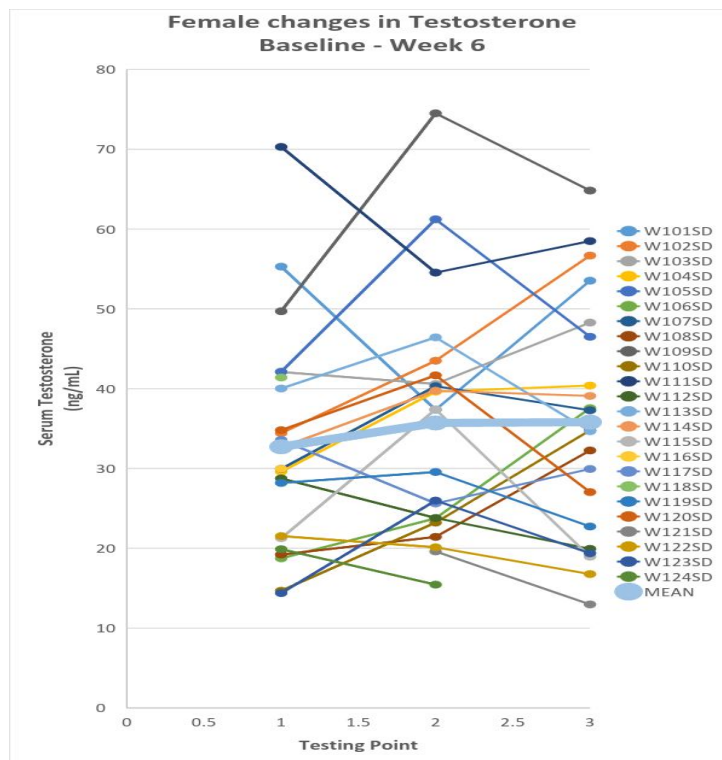
**Figure 8b:** Individual trajectories for serum cortisol concentrations are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line.



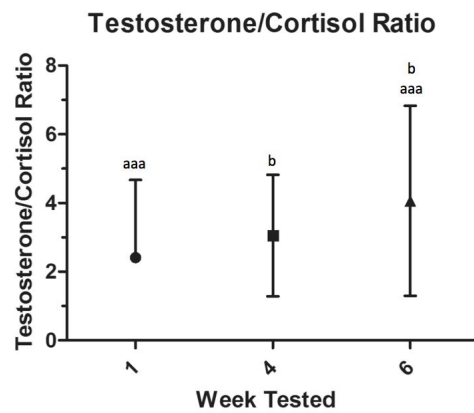
**Figure 9a:** Repeated-measures ANOVA for serum testosterone concentration. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. No significant differences noted (NS).



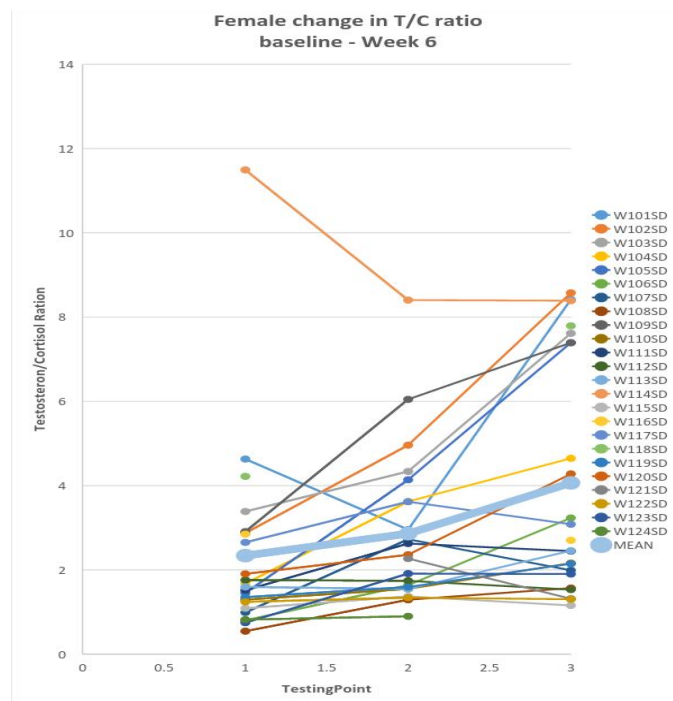
**Figure 9b:** Individual trajectories for serum testosterone concentrations are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line.



**Figure 10a:** Repeated-measures ANOVA for serum testosterone/cortisol ratio. The timepoint (Week) that the swimmers were tested is represented on the x-axis. The mean levels are represented on the y-axis, with the error bars denoting one standard deviation (SD) away from the mean. Significant differences from post-hoc analyses (Bonferroni correction) are represented on the graphs by paired letters, with the specific level of significance defined as follows: single letter (i.e. b) =  $p < 0.05$ ; triple letters (i.e. aaa) =  $p < 0.001$ .



**Figure 10b:** Individual trajectories for serum testosterone/cortisol ratio are noted in this graph. Each color represents a single swimmer. The mean value is denoted as the bold blue line.





### Discussion

Despite the training load reaching 20-hours per week, markers of muscle damage remained within normal values during the training period. Suspensions for this normal range include swimming being a low contact sport, as 88% of their workload took place in the water and only 12% weight bearing. The markers of muscle damage over the 7-weeks of testing peaked during week two reaching CK levels of  $446 \pm 723$ . This impressive spike was most likely due to week-two being the first week of training post-offseason, and depending on their training habits during the summer would be a startling change to their bodies, primarily for the weight room workouts, which included weighted bench press and squatting; both known to provoke high CK values ( Galvez et al., 2008; Moeckel-Cole & Clarkson, 2009; Stanfa et al., 2016; Smoot et al., 2013).

There was wide variability in markers of muscle damage among subjects during the course of the study. One reason for this includes the training schedules of subjects prior to the start of the study. For many, the beginning of the season was the first time they had been in the water since the end of the school year 4-months prior, while others trained consistently during the off season. This was true for a subject who reached a CK level of 3,558 U/L during the second testing, or the first week of workouts. Unfortunately, we did not evaluate diet which may have influenced the amount of muscle breakdown which occurred or genetic possibilities which may have predisposed a few of these swimmers to enhanced muscle breakdown during week 2.

It is likely that muscle soreness increased through week 5 due to the increasing duration and frequency of practices. At the beginning of training, two 6:00am practices were installed, and every two weeks increased by one so that at the end of the testing period subjects were



swimming a total of four morning practices. Overall fatigue and exhaustion had set in by week 5. After this, there was a decline in muscle soreness; most likely due to the change in practice intensity altered by the coaches to accommodate the female swimmers whom had competition during that week.

We had previously hypothesized that muscle soreness would be a good indicator of muscle damage, but that was not the case in our results. Although not statistically significant, the swimmers with the highest creatine kinase and myoglobin values seemingly had the highest ratings of muscle soreness as seen in the individual graphs (above a soreness rating of 8). This may lead us to believe that only at the uppermost ratings of soreness will soreness actually reflect muscle breakdown. At lower to mid-range ratings of muscle soreness (as seen in this study), the perceptions of both upper and lower body soreness are due to factors other than muscle cell breakdown that remain unknown. This requires future investigation.

During the testing period, cortisol went down and testosterone went up. This catabolic/anabolic relationship is an indicator of how well the athletes were responding to the training they were being subjected to. Because the testosterone/ cortisol ratio went up ( $2.4 \pm 2.3$ ;  $3.0 \pm 1.8$ ;  $4.1 \pm 2.8$ ;  $p=0.0003$ ), it can be concluded that despite the increase in swimmer soreness, they were building muscle and responding to training appropriately.

Interestingly enough, when we categorized swimmers with a CK level  $>600$  vs  $<600$ , and when myoglobin was  $>60$  vs.  $<60$ , the only difference between these two groups was in height. This would suggest that the taller swimmers were more at risk for muscle breakdown during the preseason training. The same did not apply to body weight, lean mass, or fat mass. However, we still do not understand the significance of this interesting finding.

### **Conclusion**

Muscle damage in collegiate female swimmers remained largely within the normal range (CK<200U/L) on average, but was highly variable between individuals. Significant changes were noted in CK, LS, cortisol, and T/C ratio. However, no correlations were noted between muscle damage (CK, MYO) and (upper and lower) body soreness, at moderate (2-6) ratings of muscle soreness. Serum cortisol declined over training, promoting an anabolic hormonal environment.

### **Limitations**

There were many limitations to this study, primarily the inability to control the subjects outside of the lab. This includes but is not limited to the diets (nutrition and hydration), sleep patterns, and variant school loads of each individual. These inconsistencies had the potential to alter data, and therefore should be considered in future studies.

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