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Serum Cartilage Oligomeric Matrix Protein Levels in Collegiate Soccer Athletes over the Duration of an Athletic Season: A Pilot Study

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Abstract

Objective. The primary objective of this study was to measure serum cartilage oligomeric matrix protein (sCOMP) levels weekly in a group of collegiate soccer athletes over the duration of a spring soccer season and 2 weeks following the conclusion of the season while documenting minutes of exercise participation as a measure of exercise intensity. *Design.* A repeated-measures study design was employed. A volunteer sample of 6 female soccer athletes participated in this study. Serum samples were collected on 10 separate occasions, 1 week prior to the start of the season (baseline), once a week during the 8-week season (PX1-PX8), and once a week for 2 weeks following the conclusion of the season (postseason; PS1 and PS2). Minutes of participation were documented following all spring soccer activities for each week. Once all samples were collected, sCOMP concentrations were determined using a commercially available enzyme-linked immunosorbent assay. *Results.* The results of Friedman test revealed a significant effect for time ($P = 0.003$). Post hoc analysis revealed no significant differences between baseline and practice or postseason levels. A qualitative analysis of the sCOMP levels and minutes indicated higher sCOMP levels occurred when the athletes' participation in soccer-related activities was higher. *Conclusions.* Qualitatively, our findings suggest that as minutes of participation increased, sCOMP levels increased. However, no statistically significant differences were identified. We speculate these increases were an increase in cartilage turnover and an interesting observation related to increases in physical activity. However, the implications are unclear as there was a return to near baseline levels.

Keywords

biomarkers, diagnostics, sports injury, diagnosis, articular cartilage, tissue, collegiate athletes

Introduction

While the benefits of exercise are widely known, the exact level or amount of physical activity that has a deleterious effect on articular cartilage and overall joint health has not been identified.[1,2] Biomarkers specific to articular cartilage degradation may serve as a viable indicator for determining the effects of exercise on articular cartilage. One such biomarker, cartilage oligomeric matrix protein (COMP), is a protein produced by chondrocytes and is primarily identified in articular cartilage.[3,4] Changes in synovial COMP and serum COMP (sCOMP) levels have been reported after knee injury,[5-7] in patients with osteoarthritis (OA) and varying severities of OA,[8-11] and following physical activity.[3,12-16]

Changes in sCOMP levels following bouts of physical activity have been reported.[3,12-18] Specifically, immediately following 30 minutes of walking, sCOMP levels were increased by 9.7% from baseline and returned to baseline 30 minutes postexercise.[15] In comparison, following 30 minutes of running, sCOMP levels were increased significantly from baseline immediately following the activity and returned to baseline approximately 90 minutes after activity.[14] Similarly, studies that examined more intense physical

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activity such as marathon races[3,12] and ultra-marathon races[12,18] also demonstrated increases in sCOMP levels. For marathon runners, sCOMP levels were elevated at the conclusion of the race and returned to baseline within 48 hours after the race.[3,12] In comparison, sCOMP levels for ultra-marathon runners were 1.9 times greater than baseline following the race, and returned to baseline 6 days following the race.[12] Although sCOMP levels return to baseline levels following physical activity, the rate of return may depend on the intensity of the physical activity.[3,14,15,17]

The stability of sCOMP levels has recently been studied in a group of collegiate soccer athletes during a competitive season.[16] The investigators reported that sCOMP levels were elevated when baseline was compared to the mid-season and postseason time points; however, the increases did not exceed the variability associated with the measure.[16] While these elevations were not clinically significant, it was hypothesized that the elevations of sCOMP may have been influenced by the amount of exercise participation.[16] Understanding the effects of exercise intensity on the deviation of sCOMP levels from baseline levels may provide more knowledge as to the benefits and or consequences of exercise and whether or not the amount of exercise has an effect on sCOMP levels in athletes. Therefore, the primary purpose of this study was to serially measure sCOMP levels in a group of collegiate soccer athletes over the duration of a spring soccer season and 2 weeks following the conclusion of the season. In addition, we collected minutes of participation in all soccer-related activities for the duration of the season.

Methods

Study Design

A repeated-measures study was employed for the purposes of this research investigation. The dependent variables were sCOMP (ng/mL) and exercise participation. The independent variable was time (baseline, practice sessions [PX1-PX8], and postseason [PS1 and PS2]).

Participants

A sample of 7 females volunteered for this study. One subject was removed from the analysis as she did not participate in the spring soccer season due to injury. Therefore, a total of 6 females (age = 18.8 ± 1.3 years; height = 66.5 ± 1.6 cm; mass = 67.1 ± 7.4 kg) were included in this analysis. All subjects were affiliated with the women's soccer team and participated in the spring soccer season. Subjects were excluded if they had a history of lower extremity surgery. Each subject provided informed consent prior to participation. This study was approved by the University of Kentucky Institutional Review Board.

Procedure

Subjects reported to the data collection site on 10 separate occasions for data collection. Each serum collection took place on the same day of the week at the same time of day. The first serum sample (baseline) was collected the week prior to the start of the spring soccer season. In addition, serum was collected once a week during the spring soccer season (practice; PX1-PX8). Serum was unable to be collected for week PX4 as the subjects were unavailable for data collection. Finally, serum was collected once a week for 2 weeks following the conclusion of the spring soccer season (postseason; PS1 and PS2).

During each data collection session, the subjects were asked to remain seated for 30 minutes prior to serum collection. Once seated for 30 minutes, a maximum of 10 cm^3 of whole blood was drawn from the left or right antecubital fossa using standard venipuncture procedures. Immediately after serum collection, the blood was placed on ice and transported to the laboratory for separation. After clotting for 30 minutes at room temperature, sera were separated and stored in a −80°C freezer until analysis. Once all samples were collected, sCOMP concentrations were determined using a commercial enzyme-linked immunosorbent assay (ELISA) to measure human serum or synovial intact or fragmented COMP as an indicator of COMP turnover ALPCO, Euro-Diagnostica, Malmo, Sweden, Ref. No. COMP 200). Serum COMP values were expressed as ng/mL. The average intra-assay coefficient of variance (CV) of all controls was 2.3%, the average inter-assay CV of all controls was 1.5%, and the average CV of all sample duplicates was 1.4%.

In addition, minutes of participation were documented following all spring soccer activities. Each day during the spring soccer season practice, game, weight lifting, and agility minutes were documented and totaled on a weekly basis. The activities documented were team-oriented activities in which all participants should have been in attendance. Not all activities occurred on the same day; however, all activities did occur throughout the practice session week (PX1-PX8) except games, which are limited in the spring soccer season and occur later in the spring session.

Statistical Analysis

Descriptive statisticsmedian (minimum, maximum) for sCOMP for each of the time points were calculated. A Friedman's test was employed to determine if differences in the practice (PX1-PX8) and postseason (PS1 and PS2) sCOMP values existed when compared with baseline levels. If a significant main effect was found, post-hoc analysis was performed using the Wilcoxon test. Finally, a qualitative analysis of the relationship between exercise participation (minutes) and sCOMP levels was performed. For this

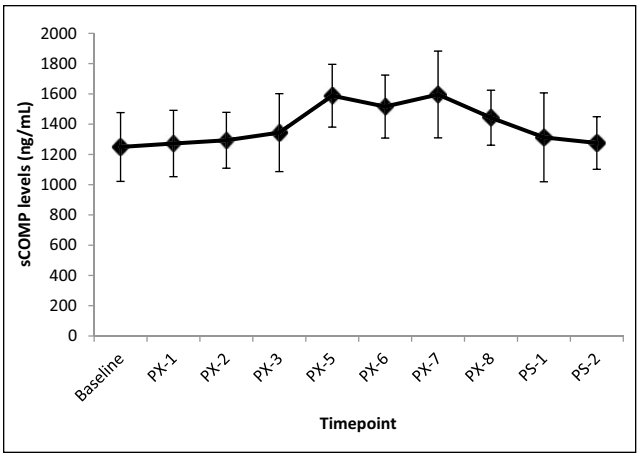

Figure 1. Serum cartilage oligomeric matrix protein (sCOMP) levels and associated 95% confidence intervals (CIs) for each of the time points (baseline, practice [PX1-PX8], postseason [PS1 and PS2]) over the duration of the spring soccer season.

Table 1. Descriptive Statistics—Median (Minimum, Maximum)—for Serum Cartilage Oligomeric Matrix Protein (sCOMP) and Total Minutes of Participation for Each of the Time Points (Baseline, Practice [PX1-PX8], Postseason [PS1 and PS2]) over the Duration of the Spring Soccer Season.

	sCOMP Levels (ng/mL)	Minutes of Participation
Baseline	1285.5 (928.4, 1483.8)	0
PX1	1302.3 (981.4, 1596.9)	330
PX2	1310.7 (1020.6, 1496.7)	495
PX3	1338.7 (1033.1, 1706.7)	540
PX5	1576.5 (1260.0, 1814.0)	510
PX6	1524.0 (1188.0, 1768.0)	420
PX7	1555.0 (1234.0, 2036.0)	750
PX8	1470.0 (1142.0, 1624.0)	405
PS1	1314.00 (922.0, 1723.0)	240
PS2	1273.8 (993.9, 1499.0)	0

analysis, we qualitatively examined sCOMP levels and minutes of participation over the course of the athletic season presented in **Figure 1**. Here, we further explored the visual increases and decreases in sCOMP, when these increases and decreases occurred during the season, and how much activity was performed over that week. α was set a priori at $P \leq 0.05$.

Results

Descriptive statistics—median (minimum, maximum)—for sCOMP levels for each time point (baseline, PX1-PX8, PS1, and PS2), along with minutes of participation for each time point can be found in **Table 1**. The average total minutes for each activity over the course of the season were as follows: lifting 94.3 minutes, agilities 66.4 minutes, practice 290 minutes, and games 77.1 minutes. However, it must be noted that the first 5 sessions do not include any game time minutes of participation as all of the game minutes occurred in the last 3 weeks of the spring soccer season. The results of the Friedman test indicated a main effect for time ($P < 0.003$). The post hoc analyses revealed no significant differences between baseline and PX1 ($P = 0.600$), baseline and PX2 ($P = 0.345$), baseline and PX3 ($P = 0.345$), baseline and PX5 ($P = 0.075$), baseline and PX6 ($P = 0.075$), baseline and PX7 ($P = 0.075$), baseline and PX8 ($P = 0.173$), baseline and PS1 ($P = 0.463$), and baseline and PS2 ($P = 0.600$).

Discussion

The primary purpose of this study was to serially measure sCOMP levels in a group of collegiate soccer athletes over the duration of a spring soccer season and 2 weeks following the conclusion of the season. In addition, we aimed to qualitatively determine the relationship between exercise intensity (minutes) and sCOMP level changes. Our primary finding was a significant main effect for time; however, there were no significant post hoc differences when comparing baselines levels to the practice or postseason levels.

Previously, we proposed that the differences between the mid-season and postseason sCOMP levels may have been due to a decrease in the amount of minutes of participation in soccer related activities.[16] Therefore, for the purposes of this investigation, we collected minutes of exercise participation and performed a qualitative assessment of sCOMP levels and minutes of participation over the course of the athletic season to determine if a relationship exists between these 2 variables (**Figure 1**, **Table 1**). Our qualitative assessment indicates sCOMP values gradually increased from baseline to week 3 (PX1-PX3) as minutes of exercise also gradually increased (**Figure 1**, **Table 1**). The sCOMP values increased rapidly from PX3 to PX5, while the minutes of participation remained relatively the same. We speculate this increase in sCOMP (244 ng/mL) occurred as the participants did not participate in organized team soccer–related activities over the 1-week break (PX4) and going from 540 minutes of activity (PX3) to 0 minutes of activity (PX4) to 510 minutes (PX5) resulted in this increase in sCOMP levels. Serum COMP levels then appear to reach a plateau at PX5, PX6, and PX7 (**Figure 1**) where week 7 has the highest total minutes of participation. In addition, it is important to note that the participants started spring game participation during PX7 and PX8, with one game occurring at the beginning of the PS1 session. Interestingly, participation in games rather than just practice, lifting, and agilities did not seem to have a large effect on the sCOMP levels. These data could indicate a cumulative effect of

exercise participation on sCOMP levels, whereas once the athlete has been exercising at a given intensity for an extended period of time, the cartilage turnover levels off. Therefore, while post hoc analysis did not reveal any significant differences between the baseline and practice sessions, minutes of participation in soccer-related activities likely contributed to the increases in sCOMP levels; but once participating at a certain level for a certain amount of time the turnover leveled off. Finally, sCOMP levels began to decrease at PX8 and PS1, where minutes of participation were similar to that of PX1, and finally returned to baseline levels at PS2 where the subjectsdid not participate in any soccer-related activities. Given that the sCOMP levels return to near baseline levels in the postseason time points (PS1 and PS2) we believe the elevations that occur are natural in response to the intensity of the exercises performed and are not detrimental to the joint.

Our group recently[16] measured sCOMP levels in a cohort of soccer players over the duration of the spring soccer season at 3 time points: preseason, mid-season, and postseason. The results indicated statistically significant elevations at the mid-season and postseason time points when compared with the preseason levels.[16] However, these elevations did not exceed the calculated minimal detectable change (MDC) value, indicating that the elevations need to be considered carefully.[16] Similar to the results from Hoch et al,[16] our qualitative analysis presented here demonstrated an elevation in sCOMP levels throughout the practice time points and more pronounced at time points PX5-PX7 when compared with baseline values (**Figure 1**). In addition to our insignificant post hoc analysis the differences at these time points (baseline and PX5 [339 ng/mL], baseline and PX6 [267.3 ng/mL], and baseline and PX7 [347.6 ng/mL]) are also not clinically meaningful when using the previously calculated MDC value.[16] Furthermore, we are able to take the previously calculated MDC of 464.6 ng/mL[16] and apply it to each individual participant for each individual data collection. When using this technique, it appears that only 2 participants had elevations from baseline that exceeded the MDC when baseline was compared with practice sessions. However, it must be noted that none of the subjects had values that exceeded the MDC when baseline values were compared with the postseason values. Thus, while there were increases outside of normal variation associated with the measure during the season, we interpret these elevations as not detrimental to joint health as the postseason values did not exceed the MDC when compared with baseline levels.

The qualitative analysis of our current data presented in **Figure 1** and **Table 1** also indicates the postseason (PS1 and PS2) sCOMP levels return to at or near baseline levels. We believe the return to baseline levels following a season of soccer-related activities indicates the elevations of sCOMP detected throughout the season are indicative of an increased cartilage turnover process that may not have an effect on long-term joint health for these 6 participants. We agree with previous research that documented increases in sCOMP levels during a marathon that returned to baseline postexercise were not indicative of pathological changes to the joint structures but changes associated with participation in physical activity.[3] However, future research and a larger sample are needed to determine the effects of exercise participation on these levels and any long-term implications of these elevations. Possibly certain individuals at risk for the development of OA may have elevated levels over the course of the season and their postseason levels may not return to baseline levels, indicating harmful cartilage turnover detected with consequences on their overall joint health.

Recently, the concept of using reference change value (RCV) to interpret COMP values given the variation of the biomarker within healthy and diseased populations has been proposed.[18-21] The RCV value represents the normal variation between each individual measurement, is calculated for each individual patient or subject, and used to interpret change specific to each individual patient or subject.[18-21] A variation of <20% of baseline is considered normal biological variation.[18,19] When using the RCV value of >20% to indicate abnormal variation in sCOMP, a total of 5 of 6 subjects had elevated levels at some point during the season compared to their baseline values. A total of 3 subjects had >20% RCV values at 4 or more time points; all occurring in the later part of the season (PX5, PX6, PX7, and PX8). However, none of the subjects had elevated levels (>20% RCV) at the postseason time points (PS1 and PS2). At this time, we speculate, based on the levels returning to <20% RCV for all subjects, the increases noted during the season were not indicative of irreversible structural changes. However, future research studies should continue to utilize the RCV values and incorporate additional documentation of joint damage and injuries sustained throughout the season in order to elucidate these documented elevations.

Throughout the literature, several studies have used distance to measure exercise.[3,12,18] However, considering we included practice, conditioning activities, agilities, and weight lifting; distance was not a practical measure of exercise participation for us to measure. Therefore, our goal was to identify a value that would incorporate all soccer-related activities. Several other investigators have used minutes to measure exercise during a single bout of activity when measuring changes in sCOMP related to exercise in healthy and OA populations.[13-15,17] Our study is the first to document repetitive bouts of activity for an entire week, for multiple weeks over the course of an athletic season. Therefore, we chose to use minutes as our measure of exercise intensity in order to capture all participation related to soccer, such as practices, games, lifting sessions, and agility sessions.

Limitations

This study is not without limitations. This study was a pilot study, therefore the sample size (n = 6) is quite small and interpretations of these data must be made with caution for each data point. We were unable to collect serum during week 4 because the athletes were not available due to spring break, and the athletes were not asked to keep records of the activities they participated in while on break. While we collected serum on the same day of the week and at the same time of the day, we did not control for activities preceding data collection. Previous injury history information, aside from surgery to the lower extremity, was not documented. Our subjects did not have a history of lower extremity surgery; however, injury history such as ankle sprain could have an effect of sCOMP levels and should be investigated. Finally, participation in activities outside of soccer was not controlled. We only documented the minutes the athletes participated in while participating in soccer-related activities (agility, weight lifting, conditioning, practice, and games). The athletes could have participated in other activities such as recreational running, and swimming. Future research should also document the amount of exercise performed while not participating in soccer-related activities.

Conclusion

To our knowledge, this is the first study to document sCOMP levels weekly in a group of collegiate soccer athletes over the course of a spring soccer season. However, our findings demonstrate insignificant changes in sCOMP levels throughout the course of an athletic season. While a significant main effect for time was present, no statistically or clinically meaningful differences were detected when comparing the baseline values to any of the practice or postseason values. The results of this study support the need for future research studies to capture a measure of exercise intensity when determining the relationship between exercise and articular cartilage damage. In addition, future research should employ a larger sample size in order to determine if our results are representative of the population of interest. We speculate the changes in sCOMP levels demonstrate increased turnover; however, it is unknown whether or not the elevations in sCOMP indicate damaging effects on overall joint health at this time. Furthermore, while our data demonstrated that all participants' sCOMP levels returned to at or near baseline levels, it is possible some individuals' levels may continue to increase; possibly representing irreversible joint damage that predisposes them to OA development. Therefore, further research is necessary to investigate the long-term implications of sCOMP elevations and exercise participation in healthy individuals such as the 6 participants included in this research study and those that have conditions that can predispose them to OA development, and the impact these elevations have on overall joint health.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by our institutional review board.

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