HHS Public Access

Author manuscript

Am J Sports Med. Author manuscript; available in PMC 2024 February 27.

Published in final edited form as:

Am J Sports Med. 2022 July ; 50(8): 2258–2270. doi:10.1177/03635465221098112.

The Role of Reported Affective Symptoms and Anxiety in Recovery Trajectories Following Sport-related Concussion

Bernadette A. D'Alonzo, MPH,

Abigail C. Bretzin, PhD, ATC,

Douglas J. Wiebe, PhD,

Ivy League–Big Ten Epidemiology of Concussion Study Investigators*

Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA, USA

Abstract

Background: There is growing awareness and clinical interest in athletes with affective symptoms following sport-related concussion (SRC), as these may contribute to overall symptoms and represent a modifiable risk factor of longer recovery. However, evidence of their effects on the entire return to play (RTP) trajectory, particularly among women and men, is limited.

Purpose: To examine the relationship between affective symptom reporting and RTP progression following SRC among a cohort of Division 1 student-athletes. We hypothesized those endorsing affective symptoms, and nervous-anxious symptom specifically, spend more time in RTP progression and recovery.

Study Design: Descriptive epidemiology study.

Setting: College varsity sports.

Methods: Using SRC data from the Ivy League-Big Ten Epidemiology of Concussion Study among varsity-athletes through February 2020, we identified the four affective symptoms from the SCAT 22-symptom-inventory. We modeled the relationship between a 4-category affective symptom variable and time-to-symptom resolution, return-to-full play (RTP), and in-RTP-progression, adjusting for non-affective symptom prevalence and concussion history. Cox regressions estimated hazard ratios for time-to-event outcomes; linear regressions estimated mean differences for continuous outcomes.

Results: In 2,077 student-athletes (men, 63.5%) with SRC, affective symptom prevalence was 47.6% and 44.3% in women and men, respectively, and nervous-anxious prevalence was 24.2% and 22.5%. In women, rates of symptom resolution and RTP were significantly lower in those with affective symptoms compared to not, and women with nervous-anxious symptom spent

*See details at end of manuscript.

Author for correspondence: Bernadette A. D'Alonzo, Department of Biostatistics, Epidemiology & Informatics, Perelman School of Medicine, University of Pennsylvania, Blockley Hall Room 905, 423 Guardian Drive, Philadelphia PA USA 19104-6021, dalonzob@pennmedicine.upenn.edu.

This study was performed at the University of Pennsylvania.

The University of Pennsylvania IRB serves as the Central Institutional Review Board for this study.

significantly longer in RTP progression. In men, rates of symptom resolution and RTP were significantly lower in those with co-occurring affective symptoms compared to not, affective symptoms were not associated with time in RTP progression.

Conclusion: Student-athletes with affective symptoms and nervous-anxious symptom exhibited delayed clinical recovery and RTP timelines; particularly for time in RTP. Symptom prevalence, concussion history contributed to this, however unmeasured confounding remains, indicated by poor model fit. This study motivates future work to explore affective symptoms and RTP timelines, considering anxiety and risk/protective factors over time.

Clinical Relevance: Longer clinical recovery for student-athletes experiencing affective and nervous-anxious symptoms following concussion may be modified with directed/targeted treatment.

Keywords

athletics; affective symptoms; anxiety; female; symptomology; traumatic brain injury; mild TBI

INTRODUCTION

Sport-related concussion (SRC) is a relatively common injury in collegiate athletic populations; from 2009-2014, SRCs accounted for 6.2% of athletic injuries across the NCAA, a 5-year injury rate of 4.47 per 10,000 athlete exposures (AEs).[51] Increases in rates over time can likely be attributed to improved detection and ease of reporting of incident cases of SRC through emergent university, athletic conference, and national-level surveillance studies,[24,37,51] in addition to developments in guidelines and protocols for managing SRC.[10,33,34]

Symptom assessment, albeit subjective, is one of the most common management practices following SRC, employed during initial injury evaluation (86.7%), and return to learn (RTL) and return to play (RTP) decision-making (57.3%) by athletic trainers in a variety of settings.[29] Subjective symptom reports that include a symptom inventory like the Sport Concussion Assessment Tool (SCAT5) are important instruments in identifying and managing athletes with concussion.[12] However, athletes report various types of symptoms following SRC. Common symptoms reported by collegiate athletes after concussion include headache (92.2%), dizziness (68.9%), difficulty concentrating (58.3%), sensitivity to light (49.1%), and loss of balance (36.7%).[50] Moreover, symptom presentation often differs in females and males.[4,5,11,19] Evidence suggests females exhibit more physical, somatic, and emotional symptoms than males.[17] Among collegiate athletes, females and those with history of concussion exhibit greater symptom severity in the initial three days following injury, relative to males,[25] warranting further exploration of symptom experiences of student-athletes in women's and men's sports separately. Further, almost one-third of collegiate athletes (30.7%; 32.6% female, 29.5% male) experience symptoms for longer than two weeks, and over 20% (23.0% female, 19.9% male) endure three or more weeks of symptoms post-concussion.[8] In sport-specific analyses, for example a sample of Division 1 ice hockey players, females demonstrated significantly longer times to symptom resolution and return to play clearance than males.[48] These findings support further study of symptom

type and duration following concussion among collegiate athletes to understand underlying mechanisms and identify appropriate and actionable management approaches.

Besides female sex, researchers suggest collegiate student-athletes with attention deficit hyperactive disorder (ADHD), history of motion sickness, and higher initial post-injury symptom scores present with greater symptom severity within two weeks following SRC.[25] In addition to these risk factors, the total number and type of reported SRC symptoms themselves may relate to recovery following SRC. For example, in one study, children with higher symptom burden, indicated by total number and severity of symptoms at time of injury had prolonged recovery, defined as symptom duration >28 days, compared to children with shorter symptom durations.[40] Similarly, in collegiate athletes with a concussion, greater symptom burden was related to longer time to symptom resolution.[38] However, limited research examines whether nature or type of symptom experience influences time to recovery outcomes (e.g. symptom resolution, return to full play) in large samples of collegiate student-athletes. This work is compelling and needed, since particularly in the presence of risk factors that are not easily modifiable during concussion management, identifying specific symptoms may aid clinicians in easing symptom severity and/or recovery time throughout treatment.

There is growing awareness and clinical interest in examining athletes who experience affective symptoms following SRC, as they may contribute to overall post-concussive symptoms and represent a potentially modifiable risk factor of longer recovery. For example, adolescents with affective symptoms including anxiety and depression, at baseline and following SRC, presented with higher symptom burden and poorer cognitive performance.[1] In a small sample of collegiate athletes, Sicard et al.[41] reported greater affective symptom burden in athletes with slower symptomatic recovery compared to asymptomatic athletes with a concussion and non-injured controls. Still, the relationship between anxiety and post-concussive symptoms remains unclear, and limited empirical evidence in the collegiate athletic setting demonstrates the potential effects of experiencing affective symptoms on the entire RTP trajectory. Importantly, previous work demonstrating that symptom presence[4,5,11,17,19] and symptom resolution[8,48] manifest differently between female and male athletes warrants independent study and analysis separately for these groups. This study aimed to test whether affective symptom reporting, and experiencing nervous-anxious symptom in isolation, is related to RTP progression following SRC in Division 1 student-athletes, and among women and men separately. We hypothesized that those endorsing affective symptoms, and the nervous-anxious symptom specifically, would spend a longer amount of time in RTP progression and have longer recovery following SRC.

MATERIALS AND METHODS

Data Source

We used data from the Ivy League-Big Ten Epidemiology of Concussion Study (Ivy-B1G Study), a prospective, multi-site, observational study and repository of student-athlete concussions across 19 Ivy League and Big Ten Universities, and include concussions reported in varsity sports through February 2020. Since 2013, athletic trainers (ATs) and research coordinators (RCs) identified athletes diagnosed with concussion across 19

participating campuses, and collected and submitted cases to the online study database registry. The data form consists of three sections pertaining to the athlete and their injury: 1) athlete demographic information, 2) circumstances and mechanism of concussion injury, and clinical information including symptomology, and 3) dates of injury, symptom resolution, and RTL and RTP outcomes. Athletes consented to participation in the study at the beginning of each academic year. The University of Pennsylvania institutional review board serves as the Central Institutional Review Board for this study. The study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies.[49] Previous publications outline the methods of the study in detail and describe the overall cohort.[13,37] Of note, here, we present our results referring to gender, and using the terms "women/men" and "athletes on women's/men's teams" throughout to reflect how data are collected in the Ivy-B1G Study. We refer to "female/male" athletes when citing previous literature.

Operational Definitions

Symptom experience: ATs and RCs recorded whether athletes experienced any symptoms from the SCAT 22-symptom inventory at any point throughout their SRC recovery. Here, we select out the four affective symptoms (more emotional, irritability, sadness, and nervous-anxious), based on the Centers for Disease Control and Prevention's Traumatic Brain Injury and Concussion symptom matrix[15,16] and previous literature,[2,26,27,35] and we compare athletes in our cohort who reported experiencing these symptoms following SRC to those who did not, stratified by gender. We also examine the recovery trajectories of women and men athletes reporting the nervous-anxious symptom, specifically.

Recovery outcomes[13,37]: We define time to the outcome symptom resolution as the number of days between date of concussion injury and date when the athlete self-reported being symptom-free. We define time to return to full play as the number of days between concussion injury and the date the athlete was medically cleared by a physician within the sports medicine or athletics department to return to full athletic participation.[8] We also report on *time in RTP progression*, calculated as the number of days between date of symptom resolution and date of return to full athletic participation, akin to when the athlete completed their stepwise RTP progression.

Statistical Analysis

We present the prevalence of SRC to date across all sports, and test for between-gender differences by class year, age, symptom burden (number of symptoms endorsed/SCAT 22-symptom inventory), and concussion history (≥1 self-reported previous-concussion(s), diagnosed by a medical provider) using Wilcoxon rank-sum tests and chi-square tests for categorical variables. To determine the internal consistency of our affective symptom domain, we calculated the Kuder-Richardson coefficient for the four affective symptoms. We used logistic regression to estimate the likelihood of reporting nervous-anxious symptom. With survival analysis we estimated time to the three outcomes of interest: 1) symptom resolution, 2) return to full play, and 3) time in RTP progression. We report the proportion of athletes whose RTP occurred on the same day(0) and before(−) reporting symptom

resolution. Crude and adjusted Kaplan-Meier (K-M) curves with Log-Rank tests presented and tested differences between symptom burden (median number of symptoms; >or≤11 symptoms) and between concussion history (≥1 previous-concussion), separately by gender. Student-athletes were censored at the end of each academic year of participation, so they may have reached their outcomes at a later date. Additional independent right censoring may have occurred in cases where athletes were lost to follow-up at the end of an athletic season or from leaving sports or school altogether. We examined K-M curves for violations of the proportional hazards assumption and assessed the correlation between the scaled Schoenfeld residuals and time using the Schoenfeld test.

We used Cox proportional hazards regressions to estimate hazard ratios (i.e., rate ratios) for symptom resolution, return to full play, and time in RTP progression during 7-weeks post-injury in women and men, separately. Our main predictor of interest was a four-level, categorical measure of experiencing symptoms in the affective domain: 1) No affective symptoms, 2) Co-occurring affective; nervous-anxious and irritability and/or sadness and/or more emotional, 3) Only nervous-anxious, 4) No-nervous-anxious; irritability and/or sadness and/or more emotional. We present crude, univariate models and include non-affective-symptom burden; the number of 18-non-affective symptoms endorsed (to mitigate the risk of multicollinearity), and concussion history (≥1) as covariates in the Cox multiple, adjusted models.

As a second analysis, we used linear regression to model crude and adjusted relationship between our four-level measure of affective domain and days in RTP progression by sex. Skewedness and kurtosis were tested to evaluate the RTP progression variable for normality. Statistical analysis was performed using Stata16.1 (StataCorp,LLC).[43]

RESULTS

SRC Prevalence

A total of 2,077 SRCs (Women, n=759; Men, n=1,318) occurred November 2013 through February 2020 across 26 varsity sports at participating sites (Supplemental Table 1). For women, the top three sports with the largest number of SRCs included soccer (n=149,19.6%), lacrosse (n=88,11.6%), and basketball (n=78,10.3%). For men, half of SRCs occurred in football (n=655,50.5%), followed by wrestling (n=127,9.6%), and lacrosse (n=124,9.4%). The distribution of SRCs was similar across class year when injured (p=0.18), with Sophomore year making up the largest proportion for women and men (n=165,29.6%; n=285,32.1%, respectively). Median age at time of SRC was different between women (median=19, IQR=19-20) and men (median=20, IQR=19-21, p<0.001). Student-athlete SRC characteristics are presented in Table 1.

Time to Recovery Outcomes

For women, median time to symptom resolution, RTP, and time in RTP progression was 10 (IQR=4-14), 14 (IQR=9-23), and 6 (IQR=4-10) days, respectively. For men, median time to symptom resolution, RTP, and time in RTP progression was 10 (IQR=3-13), 11 (IQR=9-20), 6 (IQR=4-10) days, respectively.

SRC Symptom Burden

Overall number of symptoms following SRC (symptom burden) were comparable between sexes (median=11, IQR: 7-15) (Table 1). Endorsing more symptoms (>11 symptoms) was associated with median 5-day delay in time to symptoms resolving for women (11, 6 days, p<0.0001) and men (10, 5 days, p<0.0001) (Figure 1a,1b). Stratified by concussion history, time to symptom resolution was significantly delayed among women with more symptoms (p<0.0001) (Figure 1c,1d). Women with higher symptom burden (>11 symptoms) and history of concussion demonstrated longest median time to symptom resolution (12 days). Women with lower symptom burden (≤11 symptoms) and no previous concussion exhibited shortest median time to symptom resolution (5 days). Among men, higher symptom burden and no history of concussion demonstrated the longest median time to symptom resolution (10 days). Men with lower symptom burden without history of concussion exhibited shortest median time to symptom resolution (4 days; p<0.0001).

For return to full play, having higher symptom burden (>11 symptoms) was associated with 6-day delay in women (median=17, 11 days, p<0.0001) and 4-day delay in men (median=15, 11 days, p<0.0001; Figure 2a,2b). Stratified by concussion history, women with higher symptom burden and no concussion history had the longest time to RTP (18 days). Women with lower symptom burden and no history of concussion had the shortest return to play (median=10 days, Figure 2c). Half of men with higher symptom burden with and without a history of concussion returned to play within 16 and 15 days, respectively. Men with lower symptom burden with and without a history of concussion demonstrated the fastest return to full play (12, 10 days, respectively, p=0.0001; Figure 2d). Overall, time to symptom resolution and full play among women with SRC was 1-2 days longer than men regardless of symptom burden and concussion history.

Symptom Prevalence

The most commonly reported symptoms were headache (women:96%, men:94%), pressure in the head (women:81%, men:77%), don't feel right (women:80%, men:81%) (Figure 3). Affective symptoms were among the least common with 20-40% of athletes reporting feeling more emotional, irritability, sadness, nervous-anxious following SRC. Affective symptoms had excellent internal consistency (Women, α=0.83; Men, α=0.82), meaning they are strongly correlated with each other in women and men. The number of athletes who reported at least one symptom within the affective domain was also comparable between women and men (n=265, n=394; p=0.23). The nervous-anxious symptom always co-occurred with at least 4 other symptoms from the 22-symptom-inventory for women and men. Overall, women were 40% (OR=1.40, 95%CI=1.33-1.47, p<0.001) and men 33% (OR=1.33, 95%CI=1.26-1.40, p<0.001) more likely to report nervous-anxious symptom with each additional symptom they reported.

Affective Symptom Domain

Symptoms took the longest to resolve (median=11 days) among women with co-occurring affective symptoms, and those without affective symptom endorsement exhibited the shortest time to symptom resolution (median=6 days, p<0.0001; Figure 4a). Similarly, men endorsing co-occurring affective symptoms had the longest symptom resolution time

(median=11 days), and those without affective symptoms had shorter symptom duration (median=5 days; p<0.0001; Figure 4b).

These patterns persisted for the outcome return to full play. Women with co-occurring affective symptoms demonstrated the longest time to return to full play (median=19 days). Half of women with no affective symptoms returned within 12 days (p<0.0001, Figure 4c). Men with co-occurring affective symptoms demonstrated the longest time to return to full play (19 days). Men with no affective symptoms or only nervous-anxious symptom returned to full play the earliest (median=12 days, p=0.002; Figure 4d).

Time to Symptom Resolution

Compared to women who did not experience any affective domain symptoms, the rate of symptom resolution was 30% lower (HR=0.70, 95%CI=0.54-0.91, p<0.01) for women with co-occurring affective symptoms, 36% lower (HR=0.64, 95%CI=0.40-1.04, p=0.07) for women who experienced nervous-anxious only, and 26% lower (HR=0.74, 95%CI=0.59-0.92, p<0.01) for women who experienced other affective symptoms without nervous-anxious, adjusting for symptom prevalence (HR=0.94, 95%CI=0.92-0.96, p<0.001) and history of concussion (HR=0.73, 95%C=0.61-0.87, p=0.001). For men, the adjusted model did not meet the proportional hazards assumption; complete results are presented in Table 2.

Time to Return to Full Play

Compared to women who did not experience any affective domain symptoms, the rate of return to full play was 46% lower (HR=0.54, 95%CI=0.41-0.71, p<0.001) for women with co-occurring affective symptoms, 28% lower (HR=0.72, 95%CI=0.40-1.29, p=0.27) for women who experienced nervous-anxious only, and 29% lower (HR=0.71, 95%CI=0.55-0.91, p<0.01) for women who experienced other affective symptoms without nervous-anxious, adjusting for symptom prevalence (HR=0.97, 95%CI=0.94-0.99, p<0.01) and history of concussion (HR=0.85, 95%CI=0.71-1.03, p=0.09). For men, estimated hazard ratios were 0.87 (95%CI=0.68-1.11, p=0.27) for those with co-occurring affective symptoms, 1.02 (95%CI=0.66-1.55, p=0.94) for men who experienced nervous-anxious only, and 0.99 (95%CI=0.82-1.21, p=0.95) for men who experienced other affective symptoms without nervous-anxious, adjusting for symptom prevalence (HR=0.95, 95%CI=0.93-0.97, p<0.001) and history of concussion (HR=0.87, 95%CI=0.75-1.01, p=0.07).

Time in RTP Progression

RTP was reported to have occurred on the same day as symptom resolution for 27 (1.87%) student-athletes and RTP occurred prior to symptom resolution for 12 (0.83%) student-athletes. Compared to women who did not experience any affective domain symptoms, rate of time in RTP progression was 35% lower (HR=0.65, 95%CI=0.49-0.84, p=0.001) for women with co-occurring affective symptoms, 39% lower (HR=0.61, 95%CI=0.35-1.06, p=0.08) for women who experienced nervous-anxious only, and 14% lower (HR=0.86, 95%CI=0.67-1.10, p=0.22) for women who experienced other affective symptoms without nervous-anxious, adjusting for symptom prevalence (HR=0.99,

95%CI=0.97-1.02, p=0.63) and history of concussion (HR=0.85, 95%CI=0.71-1.02, p=0.09). For men, estimated hazard ratios were 0.93 (95%CI=0.73-1.19, p=0.57) for those with co-occurring affective symptoms, 1.00 (95%CI=0.65-1.55, p=0.99) for men who experienced nervous-anxious only, and 0.99 (95%CI=0.82-1.21, p=0.95) for men who experienced other affective symptoms without nervous-anxious, adjusting for symptom prevalence (HR=0.99, 95%CI=0.97-1.01, p=0.61) and history of concussion (HR=0.87, 95%CI=0.74-1.01, p=0.06).

In the secondary analysis of number of days in RTP progression using linear regression, women who reported experiencing nervous-anxious symptom alone spent on average 38 days (β=38.46, 95%CI=7.11-69.80, p=0.02) longer in RTP progression than those who reported no affective symptoms, holding other covariates constant. Women with co-occurring affective symptoms took on average 10 additional days in RTP progression, but this was not statistically significant. For men, the measures of anxiety and days in RTP progression were not associated. For women and men, history of ≥1 previous concussion(s) was significantly associated with longer average time in RTP progression; 15 days (β=14.60, 95%CI=3.94-23.29, p<0.01, R^2=0.03) for women and 7 days (β=6.90, 95%CI=3.42-18.24, p=0.02, R^2=0.01) for men. Overall, fit of the linear models was poor; results are presented in Supplemental Table 2.

DISCUSSION

This study extends previous literature examining the influence of higher symptom burden on concussion recovery outcomes, by assessing the role of affective symptom reporting overall, and the nervous or anxious symptom alone on timelines to symptom resolution and return to full play outcomes following SRC. We explored these relationships separately among women and men in a homogenous sample of student-athletes, collected via a large, multi-site surveillance study of SRC in the Ivy League and Big Ten athletic conferences.

Our findings suggest total number of symptoms during recovery from SRC did not differ by gender, however, for both women and men, experiencing >11 symptoms endured a 5-day delay in symptom resolution compared to those with fewer symptoms. Headache, pressure in the head, and don't feel right were the most commonly reported symptoms; whereas, affective symptoms were the least common in women and men, alike, which is comparable with previous cohorts of collegiate student-athletes with SRC.[26] Although 20-40% of concussed athletes experienced affective symptoms, women and men were 40% and 33% more likely to experience nervous-anxiousness with each additional symptom endorsed, respectively. For women and men, athletes with no affective symptoms experienced the fastest median recovery; in contrast, those experiencing nervous-anxiousness that co-occurred with at least one other affective symptom demonstrated longest recovery outcomes. These results suggest total symptom burden may not be the only factor for longer recovery times following SRC, but symptom type matters, and may direct modifiable efforts to preventing prolonged recovery.

We observed a significant association between higher symptom burden paired with concussion history, and longer times to symptom resolution and return to full play for

women and men. These results are unsurprising due to previous literature suggesting that children and collegiate athletes with higher symptom burden experience longer recovery.[25,40] Other factors, including female sex, ADHD, and history of migraines may be influential in an athlete's recovery timeline,[25] however, these factors are not as easily modifiable during concussion management, warranting continued study. Regardless of these risk factors, women lag behind men in their time to symptom resolution and return to full play. These results reflect previous findings that identify sex differences in overall clinical recovery timelines.[6-8,48] Importantly, contrasting findings suggest recovery differences do not exist when controlling for injury severity,[23] level of contact and Division of play,[32] sport,[20] faster initial evaluation[36] and earlier presentation to specialized care,[21] or medical provider authorizing clearance.[9] This may highlight differences in concussion management between women and men (or even a need in women) at earlier stages and warrants further attention, as both display seemingly similar time in their RTP progression (median=6 days) in the current study. We found women with affective symptoms including experiencing nervous-anxiousness symptoms appeared in RTP progression longer than those without nervous-anxious, emphasizing the importance of identifying symptom type in addition to total symptoms to modify concussion management efforts.

Aligning with previous studies,[50] we found women and men athletes commonly experienced headache, pressure in head, don't feel right, feeling slowed down, and feeling in a fog; some researchers highlight the emotional response athletes experience post-concussion relative to controls.[30,47] In our sample, 20-40% of athletes experienced one or more affective symptoms including more emotional, irritability, sadness, and nervous-anxiousness; and the likelihood of experiencing nervous-anxiousness significantly increased with each additional symptom. A recent study examining children with pre-existing, diagnosed anxiety disorders reported greater symptom burden and delayed recovery outcomes (e.g., symptom resolution, return to school, return to physical activity) following a concussion compared to those without anxiety disorders.[31] Alternatively, Ali and colleagues[1] reported among those with diagnosed depression or anxiety, the existence of pre-morbid depression or anxiety alone did not influence post-injury cognitive or symptom recovery; yet, those with pre-existing conditions treated with antidepressants had higher symptom burden and worse cognitive scores following concussion. Although the current study didn't account for pre-existing conditions or medication (prescription or usage), we see those who report experiencing affective symptoms, including nervous-anxious symptom, demonstrate significant delays in time to symptom resolution and timelines to return to full play. A higher symptom burden overall, and importantly, the collection of affective symptoms seems to drive this delay, since endorsing the nervous-anxious symptom alone is comparable to endorsing any other of the affective symptoms. This finding supports the importance of assessing comorbid affective symptoms, as these may influence recovery outcomes following SRC. A study of healthy participants at baseline assessment demonstrated worse scores for attention and processing speed in athletes with comorbid depression or anxiety symptoms compared to controls.[44] It seems affective symptoms may also influence cognitive performance outcomes even without a concussion, indicating the presence of comorbid affective symptoms should be a consideration during concussion management.

We identified that men and women with no affective symptom experience during their SRC recovery demonstrated the fastest recovery. Specifically, men and women with no affective symptoms had a median symptom resolution in 5 and 6 days, respectively, and both returned to play in a median 12 days post-SRC. Relative to those without affective symptoms, men and women experiencing nervous-anxious alone both had a median 3-day delay in symptom resolution, and those with nervous-anxious and co-occurring affective symptoms experienced symptoms a median 4 days longer. These results align with previous literature suggesting athletes who are slow to recover from their concussion demonstrate higher affective symptom burden, measured with the Beck Depression Inventory-II (BDI-II), relative to asymptomatic concussed athletes and non-concussed control athletes.[41] In addition, in a study by Turner et al,[46] upwards of 70% of concussed athletes exceeded the threshold of clinical state anxiety, defined as a score ≥38 on the State-Trait Anxiety Inventory for Adults (STAI)[42] acutely after their injury. However, over half of athletes still displayed state anxiety above clinical thresholds at RTP, suggesting affective symptoms may last longer than other symptom subtypes.[46] Moreover, in a study of adults with concussion seen by a primary care physician or emergency department, premorbid psychiatric conditions (e.g., depression and anxiety) was a predictor of longer recovery along with older age, co-morbid personality disorders, and pre-injury health care utilization.[28] Similarly, pediatric patients, aged 12-18 years, with pre-existing, diagnosed emotional distress (e.g., depression, anxiety) exhibited longer symptom resolution relative to patients without history of depression or anxiety.[39] Importantly, the authors also reported girls and women experienced longer recovery time as well as higher percentages of pre-existing anxiety compared to males. However, this study included patients presenting to a specialty concussion clinic a median-16-days after injury. Therefore, the aforementioned studies may not be representative of student-athletes experiencing SRC in the collegiate-athletic setting. One cross-sectional between-groups study of collegiate athletes found concussion was associated with elevated anxiety, but not attentional-bias-to-threat, defined as focused awareness of threat-related stimuli, which has been considered a hallmark symptom, and in some cases, a potential causal factor of anxiety.[14] Authors suggest this has important implications for understanding not just the nature and source of anxiety following concussion, but best treatment and they urge for further studies to investigate these complex relationships.[14] Alternatively, Covassin et al.[18] demonstrated the importance of social support in mitigating state-anxiety after concussion, as concussed athletes with greater satisfaction with social support had lower state-anxiety levels, particularly at RTP-time in concussed athletes. Further, in a qualitative study, Todd et al[45] showed how ice hockey players experienced extreme feelings of compromised identity following concussion, exacerbated by feelings of isolation and stigmatization. Participants cited support from peers, family, and health care providers as key to their success moving forward after injury.[45] Therefore, adding social support and psychological intervention practices integrated into concussion management may benefit athletes, especially with affective and persisting symptoms.

These findings also have important implications for detection and identification for treatment, since feeling nervous or anxious or rather, anxiety itself, has clear screening, diagnostic, and management protocols that can be integrated into concussion management.

Still, existing studies that have evaluated affective symptoms, and anxiety specifically, following concussion, have focused on the acute post-concussion period; few have considered the role of pre-injury or long-term symptoms.[3,22] Thus, additional work is needed to determine the appropriate type and timing of affective symptom assessments, and how they can best be applied in different settings and contexts, alongside clinical judgment. However, in contexts where formal screening and/or diagnostic measures may not be feasible, it may prove useful to first utilize and inspect symptom assessment tools used during SRC management (e.g., SCAT 22-symptom-inventory) to help identify athletes following SRC who may be at-risk for prolonged symptoms and recovery, as demonstrated here.

Limitations

Our study makes important contributions by examining the role of affective symptoms on timelines to symptom resolution, RTP, and time within RTP progression following SRC, highlighting key differences among athletes in women's and men's sports, yet some limitations must be considered. In modeling the relationship between experiencing symptoms in the affective domain and time to symptom resolution, among men, our Cox multiple regression model did not meet the proportionality assumption, thus our estimate of the rate ratio cannot be assumed to be constant throughout follow-up time. For the outcome time in RTP progression, linear regression models demonstrated poor fit among women (R^2=0.03) and men (R^2=0.01), suggesting that there are additional, uncontrolled factors contributing to time in RTP progression among athletes with anxiety. This warrants continued study of student-athletes experiencing longer recovery, to identify potential preventative/actionable factors. We were not able to consider pre-existing mental health conditions, anxiety/depression screening assessments, or previous/current receipt of mental health services; future research should consider their relationship with recovery outcomes. We were limited to considering symptom burden, since symptom data from the Ivy-B1G Study are collected via a dichotomized checklist from the SCAT 22-symptom inventory. We hope this analysis inspires future examinations of symptom severity among those who endorse affective symptoms. In addition, consideration should be given to the temporality of experiencing the nervous-anxious symptom and time-dependency of this exposure and potential covariates; it may be that higher symptom burden and/or experiencing symptoms over a longer period of time exacerbates feelings of nervous-anxiousness and/or anxiety. Attention should also be given to potential source(s) of nervous-anxiousness; in particular, whether it be related to the athlete's injury and/or return to play.

The Ivy League and Big Ten conferences include programs where SRC detection and management protocols are enforced, requiring immediate removal of athletes with suspected or reported SRC, and injured athletes are progressed through RTP protocols. Therefore, this study extends research on patients presenting to emergency departments, primary care, and specialty clinics; while limiting the generalizability beyond similar athletic conferences to other competitive divisions and levels of play.

Conclusion

Affective symptom endorsement was relatively common in collegiate athletes following SRC, and these symptoms do play a role in delayed clinical recovery and return to play. Differences were evident among both women and men athletes, particularly with total time in RTP progression. Collegiate sports are a unique setting where the breadth and timeliness of healthcare resources post-injury may differ compared to previous studies of patients seeking care for prolonged symptoms at specialty clinics. By identifying the nature and extent of collegiate athletes who experience affective and nervous-anxious symptoms following SRC, we afford clinical care teams opportunities to prioritize and mobilize mental health resources, and tailor treatments to athletes. The factors measured here (gender, symptom prevalence, concussion history) contribute to this relationship; however, significant unmeasured confounding remains, indicated by poor fit in our Cox and linear models. This study establishes a precedent for future work to explore affective symptoms and RTP timelines, considering the role of anxiety and other risk/protective factors collected over time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Appendix

Ivy League-Big Ten Epidemiology of Concussion Study Investigators: Current and past site investigators have been instrumental in accomplishing this work (listed alphabetically by institution): Russell Fiore, MEd, ATC, Matthew Culp, MA, ATC, and Bryn VanPatten, PhD, MSEd, ATC (Brown University); William N. Levine, MD, and Natasha Desai, MD (Columbia University); David C Wentzel, DO and Amy Sucheski-Drake, MD (Cornell University); Kristine A. Karlson, MD (Dartmouth College); Frank Wang, MD and Lars Richardson, MD, PhD (Harvard University); Nicholas L Port, PhD (Indiana University); Mathew Saffarian, DO (Michigan State University); Brian Vesci, MA, ATC (Northwestern University); Michael Gay, PhD, ATC (The Pennsylvania State University); Carly Day, MD (Purdue University); Margot Putukian, MD and Shasha Steinlight, MD (Princeton University); Carrie Esopenko, PhD (Rutgers University); Matthew B. Wheeler, PhD, and Randy A Ballard, ATC (University of Illinois); Andy Peterson, MD, MSPH (University of Iowa); David Klossner, PhD (University of Maryland); Erin M Moore, MEd, ATC (University of Minnesota); Art Maerlender, PhD, and Cary R Savage, PhD (University of Nebraska-Lincoln); Brian J Sennett, MD (University of Pennsylvania); Erin McQuillan, MS, ATC (University of Wisconsin); and Andrew Gotlin, MD, and Stephanie Arlis-Mayor, MD (Yale University).

REFERENCES

1. Ali M, Asghar N, Li A, et al. Incidence of concussion and recovery of neurocognitive dysfunction on ImPACT assessment among youth athletes with premorbid depression or anxiety taking antidepressants. J Neurosurg Pediatr. 2021:1–7.

2. Anderson M, Petit KM, Bretzin AC, et al. Sport Concussion Assessment Tool Symptom Inventory: Healthy and Acute Postconcussion Symptom Factor Structures. J Athl Train. 2020;55(10):1046–1053. [PubMed: 33108797]
3. Arnett PA, Guty E, Bradson M. Assessment of depression and anxiety in sports concussion evaluations. American Psychological Association. 2019.
4. Baker JG, Leddy JJ, Darling SR, et al. Gender Differences in Recovery From Sports-Related Concussion in Adolescents. Clin Pediatr (Phila). 2016;55(8):771–775. [PubMed: 26378093]
5. Berz K, Divine J, Foss KB, et al. Sex-specific differences in the severity of symptoms and recovery rate following sports-related concussion in young athletes. Phys Sportsmed. 2013;41(2):58–63.
6. Bretzin AC, Covassin T, Fox ME, et al. Sex Differences in the Clinical Incidence of Concussions, Missed School Days, and Time Loss in High School Student-Athletes: Part 1. Am J Sports Med. 2018;46(9):2263–2269. [PubMed: 29879362]
7. Bretzin AC, Covassin T, Wiebe DJ, Stewart W. Association of Sex With Adolescent Soccer Concussion Incidence and Characteristics. JAMA Netw Open. 2021;4(4):e218191. [PubMed: 33904911]
8. Bretzin AC, Esopenko C, D'Alonzo BA, Wiebe DJ. Clinical Recovery Timelines following Sport-Related Concussion in Men's and Women's Collegiate Sports. Journal of Athletic Training. 2021.
9. Bretzin AC, Zynda AJ, Wiebe DJ, Covassin T. Time to Authorized Clearance from Sport-Related Concussion: The Influence of Healthcare Provider and Medical Facility. J Athl Train. 2020.
10. Broglio SP, Cantu RC, Gioia GA, et al. National Athletic Trainers' Association Position Statement: Management of Sport Concussion. Journal of Athletic Training. 2014;49(2):245–265. [PubMed: 24601910]
11. Broshek DK, Kaushik T, Freeman JR, et al. Sex differences in outcome following sports-related concussion. J Neurosurg. 2005;102(5):856–863. [PubMed: 15926710]
12. Bruce JM, Thelen J, Meeuwisse W, et al. Use of the Sport Concussion Assessment Tool 5 (SCAT5) in professional hockey, part 2: which components differentiate concussed and non-concussed players? British Journal of Sports Medicine. 2021;55(10):557–565.
13. Campbell-McGovern C, D'Alonzo BA, Cooper M, Putukian M, Wiebe DJ. Ivy League-Big Ten Epidemiology of Concussion Study. Inj Prev. 2018;24(4):319–320. [PubMed: 29706596]
14. Carlson JM, Kangas KJ, Susa TR, Fang L, Moore MT. Sport-related concussion is associated with elevated anxiety, but not attentional bias to threat. Brain Inj. 2020;34(3):363–368. [PubMed: 32050803]
15. CDC CfDCP. Report to Congress on mild traumatic brain injury in the United States: steps to prevent a serious public health problem. 2003.
16. CDC CfDCP. Surveillance Report of Traumatic Brain Injury-related Emergency Department Visits, Hospitalizations, and Deaths—United States, 2014. 2019.
17. Clair R, Levin Allen S, Goodman A, McCloskey G. Gender differences in quality of life and symptom expression during recovery from concussion. Appl Neuropsychol Child. 2020;9(3):206–214. [PubMed: 30822135]
18. Covassin T, Crutcher B, Bleecker A, et al. Postinjury anxiety and social support among collegiate athletes: a comparison between orthopaedic injuries and concussions. J Athl Train. 2014;49(4):462–468. [PubMed: 24673237]
19. Covassin T, Elbin RJ, Bleecker A, Lipchik A, Kontos AP. Are There Differences in Neurocognitive Function and Symptoms Between Male and Female Soccer Players After Concussions? The American Journal of Sports Medicine. 2013;41(12):2890–2895. [PubMed: 24197616]
20. Covassin T, Moran R, Elbin RJ. Sex Differences in Reported Concussion Injury Rates and Time Loss From Participation: An Update of the National Collegiate Athletic Association Injury Surveillance Program From 2004-2005 Through 2008-2009. J Athl Train. 2016;51(3):189–194. [PubMed: 26950073]
21. Desai N, Wiebe DJ, Corwin DJ, et al. Factors Affecting Recovery Trajectories in Pediatric Female Concussion. Clin J Sport Med. 2019;29(5):361–367. [PubMed: 31460948]
22. Gornall A, Takagi M, Morawakage T, Liu X, Anderson V. Mental health after paediatric concussion: a systematic review and meta-analysis. Br J Sports Med. 2021;55(18):1048–1058. [PubMed: 33926965]

23. Hannah TC, Li AY, Spiera Z, et al. Sex-Related Differences in the Incidence, Severity, and Recovery of Concussion in Adolescent Student-Athletes Between 2009 and 2019. Am J Sports Med. 2021;49(7):1929–1937. [PubMed: 33955795]
24. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. J Athl Train. 2007;42(2):311–319. [PubMed: 17710181]
25. Houck Z, Asken B, Bauer R, Clugston J. Predictors of post-concussion symptom severity in a university-based concussion clinic. Brain Inj. 2019;33(4):480–489. [PubMed: 30626213]
26. Joyce AS, Labella CR, Carl RL, Lai JS, Zelko FA. The Postconcussion Symptom Scale: utility of a three-factor structure. Med Sci Sports Exerc. 2015;47(6):1119–1123. [PubMed: 25268538]
27. Langdon S, Königs M, Adang EAMC, Goedhart E, Oosterlaan J. Subtypes of Sport-Related Concussion: a Systematic Review and Meta-cluster Analysis. Sports Medicine. 2020;50(10):1829–1842. [PubMed: 32720230]
28. Langer LK, Alavinia SM, Lawrence DW, et al. Prediction of risk of prolonged post-concussion symptoms: Derivation and validation of the TRICORDRR (Toronto Rehabilitation Institute Concussion Outcome Determination and Rehab Recommendations) score. PLoS Med. 2021;18(7):e1003652. [PubMed: 34237056]
29. Lempke LB, Schmidt JD, Lynall RC. Athletic Trainers' Concussion-Assessment and Concussion-Management Practices: An Update. Journal of Athletic Training. 2020;55(1):17–26. [PubMed: 31855075]
30. Mainwaring LM, Hutchison M, Bisschop SM, Comper P, Richards DW. Emotional response to sport concussion compared to ACL injury. Brain Inj. 2010;24(4):589–597. [PubMed: 20235761]
31. Martin AK, Petersen AJ, Sesma HW, et al. Concussion symptomology and recovery in children and adolescents with pre-existing anxiety. J Neurol Neurosurg Psychiatry. 2020;91(10):1060–1066. [PubMed: 32788258]
32. Master CL, Katz BP, Arbogast KB, et al. Differences in sport-related concussion for female and male athletes in comparable collegiate sports: a study from the NCAA-DoD Concussion Assessment, Research and Education (CARE) Consortium. Br J Sports Med. 2021;55(24):1387–1394. [PubMed: 33355211]
33. Mccrory P, Meeuwisse W, Dvorak J, et al. Consensus statement on concussion in sport—the 5thinternational conference on concussion in sport held in Berlin, October 2016. British Journal of Sports Medicine. 2017:bjsports-2017-2010.
34. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. British Journal of Sports Medicine. 2013;47(5):250. [PubMed: 23479479]
35. Nelson LD, Kramer MD, Patrick CJ, McCrea MA. Modeling the Structure of Acute Sport-Related Concussion Symptoms: A Bifactor Approach. Journal of the International Neuropsychological Society : JINS. 2018;24(8):793–804. [PubMed: 30079858]
36. Pratile T, Marshall C, DeMatteo C. Examining how time from sport-related concussion to initial assessment predicts return-to-play clearance. Phys Sportsmed. 2021:1–9.
37. Putukian M, D'Alonzo BA, Campbell-McGovern CS, Wiebe DJ. The Ivy League-Big Ten Epidemiology of Concussion Study: A Report on Methods and First Findings. Am J Sports Med. 2019;47(5):1236–1247. [PubMed: 30943078]
38. Putukian M, Riegler K, Amalfe S, Bruce J, Echemendia R. Preinjury and Postinjury Factors That Predict Sports-Related Concussion and Clinical Recovery Time. Clin J Sport Med. 2021;31(1):15–22. [PubMed: 30540572]
39. Rosenbaum PE, Locandro C, Chrisman SPD, et al. Characteristics of Pediatric Mild Traumatic Brain Injury and Recovery in a Concussion Clinic Population. JAMA Netw Open. 2020;3(11):e2021463. [PubMed: 33196804]
40. Schilling S, Mansour A, Sullivan L, et al. Symptom Burden and Profiles in Concussed Children with and without Prolonged Recovery. Int J Environ Res Public Health. 2020;17(1).
41. Sicard V, Harrison AT, Moore RD. Psycho-affective health, cognition, and neurophysiological functioning following sports-related concussion in symptomatic and asymptomatic athletes, and control athletes. Sci Rep. 2021;11(1):13838. [PubMed: 34226626]

42. Spielberger C, Gorsuch R, Lushene R. State-Trait Anxiety Inventory for Adults. Consulting Psychologists Press. 1970.
43. StataCorp. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. 2019.
44. Thomas GA, Guty ET, Riegler KE, Arnett PA. Comorbid Affective Symptomatology and Neurocognitive Performance in College Athletes. Journal of the International Neuropsychological Society : JINS. 2021:1–11.
45. Todd R, Bhalerao S, Vu MT, Soklaridis S, Cusimano MD. Understanding the psychiatric effects of concussion on constructed identity in hockey players: Implications for health professionals. PLoS One. 2018;13(2):e0192125. [PubMed: 29466377]
46. Turner S, Langdon J, Shaver G, et al. Comparison of Psychological Response between Concussion and Musculoskeletal Injury in Collegiate Athletes. Sport Exerc Perform Psychol. 2017;6(3):277–288. [PubMed: 29250458]
47. Valovich Mcleod TC, Wagner AJ, Bacon CEW. Lived Experiences of Adolescent Athletes Following Sport-Related Concussion. Orthopaedic Journal of Sports Medicine. 2017;5(12):232596711774503.
48. Van Pelt KL, Caccese JB, Eckner JT, et al. Detailed description of Division I ice hockey concussions: Findings from the NCAA and Department of Defense CARE Consortium. J Sport Health Sci. 2021;10(2):162–171. [PubMed: 33453430]
49. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The Lancet. 2007;370(9596):1453–1457.
50. Wasserman EB, Kerr ZY, Zuckerman SL, Covassin T. Epidemiology of Sports-Related Concussions in National Collegiate Athletic Association Athletes From 2009-2010 to 2013-2014: Symptom Prevalence, Symptom Resolution Time, and Return-to-Play Time. Am J Sports Med. 2016;44(1):226–233. [PubMed: 26546304]
51. Zuckerman SL, Kerr ZY, Yengo-Kahn A, et al. Epidemiology of Sports-Related Concussion in NCAA Athletes From 2009-2010 to 2013-2014: Incidence, Recurrence, and Mechanisms. Am J Sports Med. 2015;43(11):2654–2662. [PubMed: 26330572]

What is known about the subject:

Female and male student-athletes display different symptom experiences following concussion. Whether certain types of symptoms, specifically affective symptoms that are potentially modifiable, impact symptom resolution and return to play outcomes has yet to be explored.

What this study adds to existing knowledge:

Student-athletes with affective symptoms and the nervous-anxious symptom following SRC exhibited delays in clinical recovery and return to play timelines. Factors contributing to longer recovery outcomes included symptom prevalence, and concussion history in women and men; however, a large amount of unmeasured confounding remains.

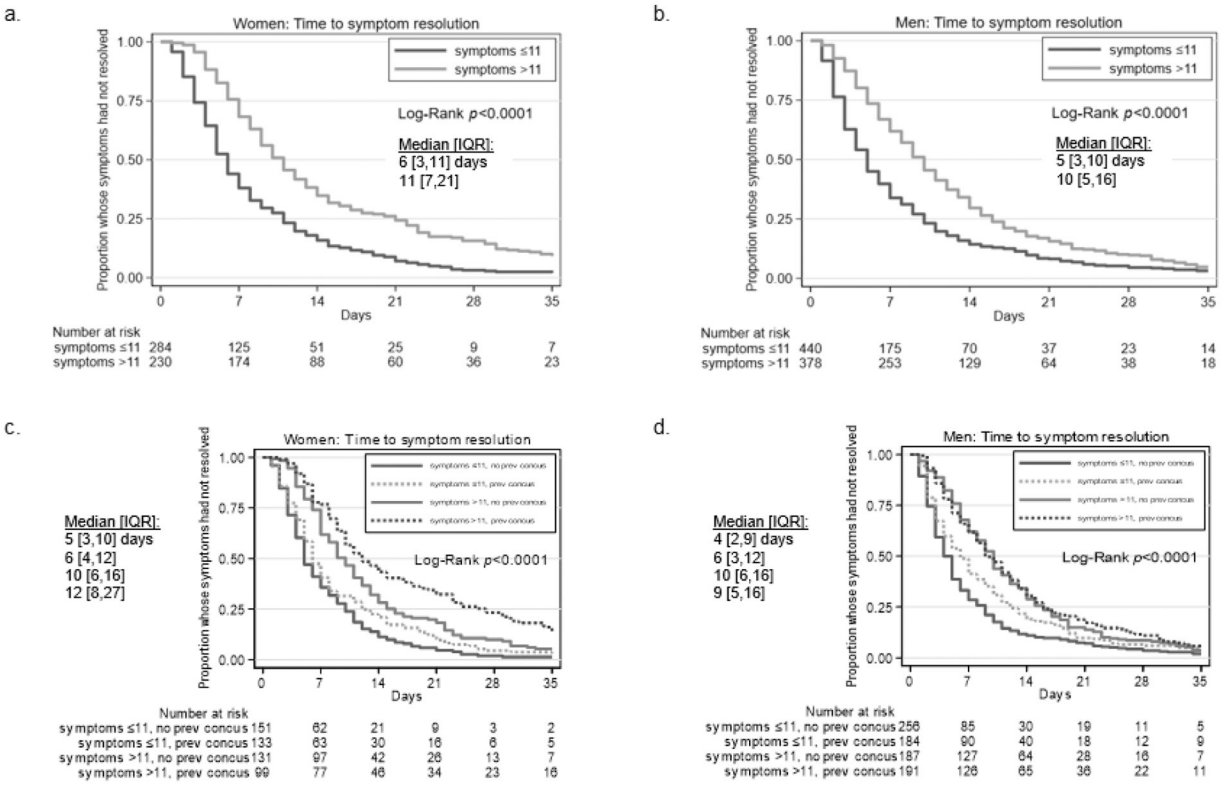

Figure 1.

Kaplan-Meier survival curves showing differences in time to symptom resolution for a. women with >11 symptoms (11 vs 6 days); b. men with >11 symptoms (10 vs 5 days); and for c. women with >11 symptoms and ≥1 previous concussion(s) (12 days), ≤11 symptoms and no previous concussions (5 days); d. men with >11 symptoms and no previous concussions (10 days), ≤11 symptoms and ≥1 previous concussion(s) (4 days). Median days and interquile ranges [IQR] are presented for the outcome symptom resolution. Log-Rank tests compare differences by symptom burden and concussion history.

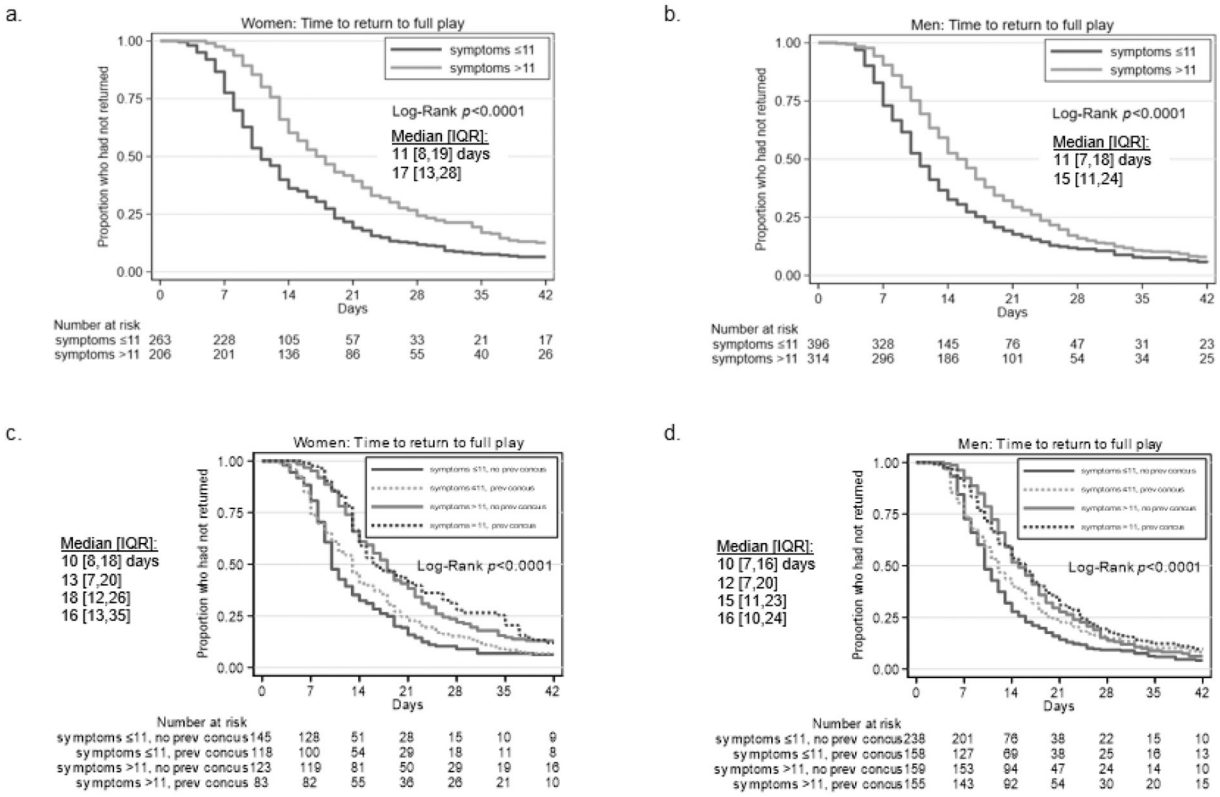

Figure 2.

Kaplan-Meier survival curves showing differences in time to return to full play for a. women with >11 symptoms (17 vs 11 days); b. men with >11 symptoms (15 vs 11 days); and for c. women with >11 symptoms and no previous concussions (18 days), ≤11 symptoms and no previous concussions (10 days); d. men with >11 symptoms and ≥1 previous concussion(s) (16 days), ≤11 symptoms and no previous concussions (10 days). Median days and interquile ranges [IQR] are presented for the outcome return to full play. Log-Rank tests compare differences by symptom burden and concussion history.

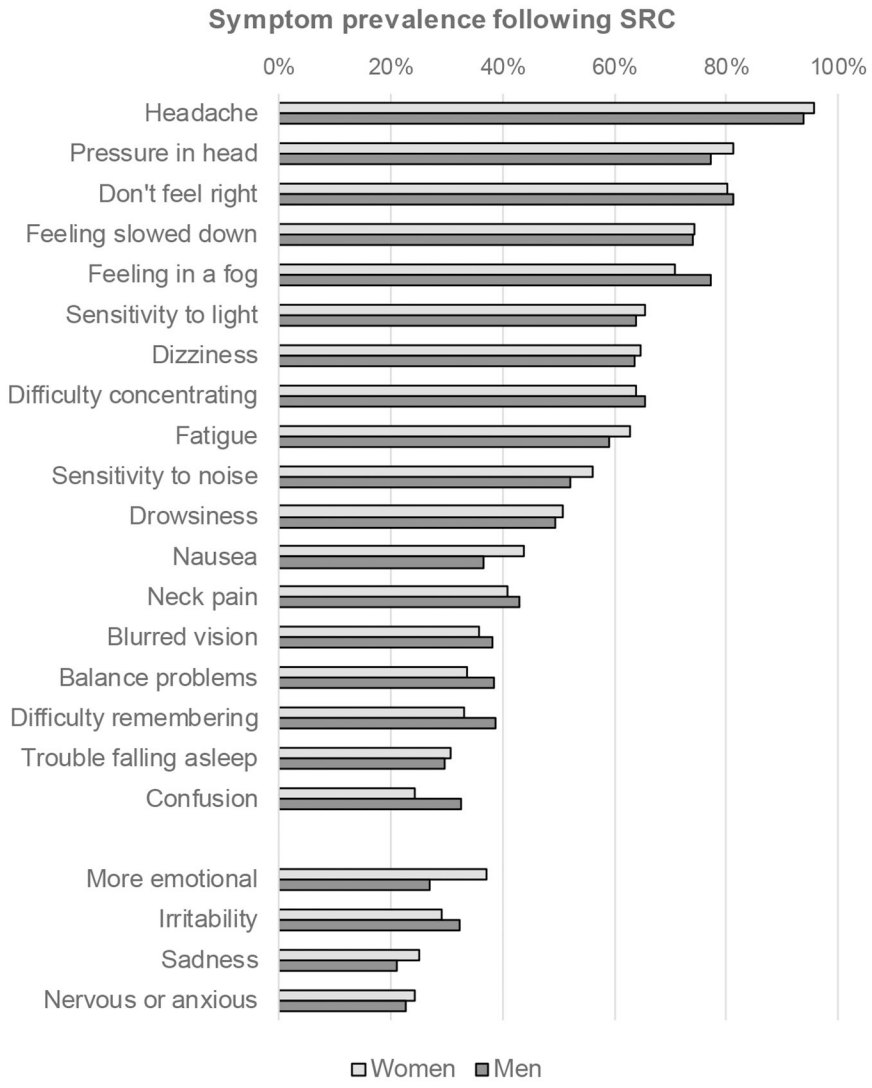

Figure 3.
Symptom prevalence among women and men. Symptoms are from the SCAT 22-symptom inventory.

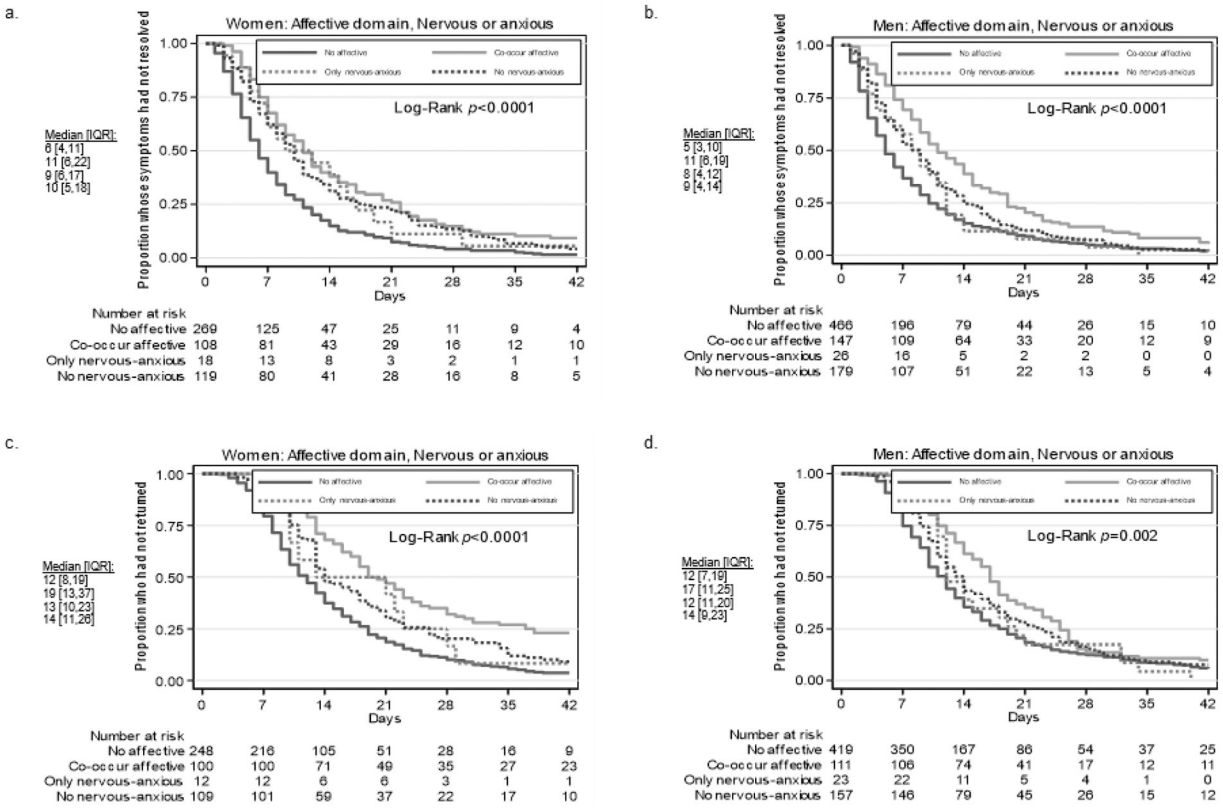

Figure 4.

Kaplan-Meier survival curves showing differences in time to symptom resolution for a. women with co-occurring affective symptoms (11 days), no affective symptoms (6 days); b. men with co-occurring affective symptoms (11 days), no affective symptoms (5 days); and return to full play for c. women with co-occurring saffective symptoms (19 days), no affective symptoms (12 days); d. men with co-occurring affective symptoms (19 days), no affective symptoms (12 days) or only nervous-anxious symptom (12 days). Median days and interquile ranges [IQR] are presented for the outcomes symptom resolution and return to full play. Log-Rank tests compare differences by affective domain category.

Table 1.

Student Athlete SRC Characteristics

Characteristic	Women	Men	p-value*
Total, #(%)	759 (36.5)	1318 (63.5)	
Class year, #(%)			
Freshman	231 (30.6)	324 (24.8)	0.031
Sophomore	218 (28.8)	406 (31.0)	
Junior	176 (23.3)	324 (24.8)	
Senior	126 (16.7)	235 (18.0)	
5th year	5 (0.7)	20 (1.5)	
Age (median, IQR)	19 (19-20)	20 (19-21)	<0.001
Symptom burden (median, IQR)	11 (7-15)	11 (7-15)	0.93
Affective symptom domain, #(%)**	265 (47.6)	394 (44.3)	0.23
Nervous or anxious symptom	135 (24.2)	200 (22.5)	0.45
Concussion history			
Yes	261 (46.9)	420 (47.2)	0.89
No	296 (53.1)	469 (52.8)	

*Chi-square test; Wilcoxon rank sum test

**Affective domain symptoms: irritability, sadness, more emotional, and nervous or anxious

Table 2.

Cox proportional hazards regression -- Breslow method for ties

2.1 Outcome: time to symptom resolution						
	Women			**Men**		
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Univariate Cox regression						
Affective domain						
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.53	0.42-0.66	<0.001	0.58 *	0.48-0.70	<0.001
Only nervous-anxious	0.63	0.39-1.01	0.39	0.87	0.59-1.30	0.50
No nervous-anxious	0.63	0.50-0.78	<0.001	0.78 *	0.66-0.93	0.01
Symptom prevalence (18)	0.93	0.91-0.95	<0.001	0.93 *	0.92-0.95	<0.001
Concussion history (1+)	0.76	0.64-0.91	<0.01	0.84	0.73-0.96	0.01
Cox multiple regression						
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Affective domain				*		
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.70	0.54-0.91	<0.01	0.79	0.64-0.98	0.03
Only nervous-anxious	0.64	0.40-1.04	0.07	0.93	0.62-1.38	0.71
No nervous-anxious	0.74	0.59-0.92	<0.01	0.95	0.79-1.14	0.62
Symptom prevalence (18)	0.94	0.92-0.96	<0.001	0.94 *	0.92-0.96	<0.001
Concussion history (1+)	0.73	0.61-0.87	0.001	0.83	0.73-0.96	0.01
2.2 Outcome: time to return to full play						
	Women			**Men**		
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Univariate Cox regression						
Affective domain						
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.46	0.36-0.59	<0.001	0.68	0.55-0.83	<0.001
Only nervous-anxious	0.72	0.40-1.28	0.26	0.91	0.60-1.39	0.67
No nervous-anxious	0.64	0.51-0.80	<0.001	0.86	0.71-1.03	0.10
Symptom prevalence (18)	0.94 *	0.92-0.96	<0.001	0.95 *	0.93-0.96	<0.001
Concussion history (1+)	0.89	0.74-1.07	0.22	0.87	0.75-1.01	0.07
Cox multiple regression						
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Affective domain						
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.54	0.41-0.71	<0.001	0.87	0.68-1.11	0.27
Only nervous-anxious	0.72	0.40-1.29	0.27	1.02	0.66-1.55	0.94
No nervous-anxious	0.71	0.55-0.91	<0.01	0.99	0.82-1.21	0.95

Symptom prevalence (18)	0.97	0.94-0.99	<0.01	0.95*	0.93-0.97	<0.001
Concussion history (1+)	0.85	0.71-1.03	0.09	0.87	0.75-1.01	0.07

2.3 Outcome: days in RTP progression

	Women			Men		
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Univariate Cox regression						
Affective domain						
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.63*	0.50-0.80	<0.001	0.91	0.74-1.12	0.38
Only nervous-anxious	0.59	0.34-1.01	0.06	1.00	0.65-1.53	0.99
No nervous-anxious	0.85	0.67-1.07	0.16	0.97	0.80-1.16	0.72
Symptom prevalence (18)	0.97	0.95-0.99	0.02	0.99	0.97-1.01	0.31
Concussion history (1+)	0.87	0.72-1.04	0.13	0.86	0.74-1.00	0.06
Cox multiple regression						
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Affective domain						
No affective	ref	ref	ref	ref	ref	ref
Co-occur affective	0.65	0.49-0.84	0.001	0.93	0.73-1.19	0.57
Only nervous-anxious	0.61	0.35-1.06	0.08	1.00	0.65-1.55	0.99
No nervous-anxious	0.86	0.67-1.10	0.22	0.99	0.82-1.21	0.95
Symptom prevalence (18)	0.99	0.97-1.02	0.63	0.99	0.97-1.01	0.61
Concussion history (1+)	0.85	0.71-1.02	0.09	0.87	0.74-1.01	0.06

Abbreviation: CI=confidence interval; HR=hazard ratio

*Did not meet proportional-hazards assumption