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Sex-Related Differences in the Incidence, Severity, and Recovery of Concussion in Adolescent Student-Athletes Between 2009 and 2019

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Background: The sex of an athlete is thought to modulate concussion incidence; however, the effects of sex on concussion severity and recovery are less clear.

Purpose: To evaluate sex differences in concussion severity and recovery using a large, heterogeneous sample of young student-athletes with the goal of understanding how sex affects concussion outcomes in young athletes.

Study Design: Cohort study; Level of evidence, 3.

Methods: The Immediate Post-Concussion Assessment and Cognitive Testing results of 11,563 baseline and 5216 postinjury tests were used to calculate the incidence of concussion of adolescent male and female student-athletes ages 12 to 22 years (median, 15 years). The postinjury tests of 3465 male and 1751 female student-athletes evaluated for concussion or head trauma were used to assess differences in the Severity Index (SI) and recovery. Chi-square tests and *t* tests were used to compare differences in demographic characteristics, incidence, and SI between the 2 cohorts. Multivariable linear, logistic, and Cox proportional hazards regressions were used to control for differences between cohorts in analyses of incidence, SI, and recovery.

Results: When we controlled for demographic differences, female participants had higher odds of concussion (odds ratio, 1.62; 95% CI, 1.40-1.86; $P < .0001$) and higher SI after concussion ($\beta = 0.67$; 95% CI, 0.02-1.32; $P = .04$). This discrepancy in SI was a result of differences in Symptom (2.40 vs 2.94; $P < .0001$) and Processing Speed (0.91 vs 1.06; $P = .01$) composite scores between male and female participants, respectively. We found no effect of sex on time to recovery when controlling for initial concussion SI (hazard ratio, 0.94; 95% CI, 0.78-1.12; $P = .48$).

Conclusion: Using large, multisport cohorts, this study provides evidence that female athletes are at higher risk for more concussions and these concussions are more severe, but male and female athletes have similar recovery times when the analysis controls for initial concussion SI.

Keywords: concussion; female athletes; ImPACT; Severity Index

Concussion or mild traumatic brain injury (mTBI) in youth sports continues to be a concern in the United States, with an estimated 1.6 to 3.8 million annual injuries.[26] Despite concerns, participation in youth sports continues to be popular due to significant physical, lifestyle, and cognitive benefits.[2] Thus, fully characterizing risk factors for concussion and minimizing their effects is important. Multiple factors including sex, player position, level of play, aggressive behavior, and environment are thought to modulate concussion risk and outcomes.[1]

Participation of women and girls in sports has significantly increased over the past few decades. During the 2018-2019 school year, 3.4 million out of 7.9 million high school athletes were female.[37] Numerous studies have examined sex differences in concussion incidence and recovery, and most agree that female athletes experience

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a higher incidence of concussion when playing the same sport as male athletes.[50] However, the existence of sex differences in concussion recovery is disputed.[50] Additionally, few studies have directly quantified the full neurocognitive severity of initial concussion.

This study examines sex-related differences in concussion incidence and recovery after concussion in young athletes through use of the Severity Index (SI), a new prognostic tool for assessing head trauma and concussion severity based on Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).[22] We hypothesized that female participants would demonstrate worse outcomes in all 3 domains. With a large cohort, consisting of 10 years of patient data across multiple sports, this study aims to advance our understanding of how the sex of the athlete affects concussion in young athletes.

METHODS

Data Collection and Head Trauma

A total of 25,815 ImPACT tests conducted between 2009-2019 were provided through a research agreement with ImPACT Applications Inc. The participants ranged in age from 12 to 22 years; the median age was 15 years. All 11,563 baseline tests were used to calculate incidence. Of these participants, 3465 male and 1751 female athletes were evaluated for head trauma and/or concussion during the experimental period. The athletic organizations in this study followed standardized protocols for evaluation of head traumas that included baseline ImPACT testing. After injury, participants were evaluated by a qualified member of the athletic staff and, if concussion could not be ruled out, were subsequently referred for an initial postinjury ImPACT assessment (PI1). These tests were used to qualify and quantify the initial SI of head trauma and/or concussion. In total, 1192 male and 672 female patients met criteria for concussion. Of these, 824 male and 427 female patients presented for a follow-up postinjury test (PI2), which was used to assess recovery. Institutional review board approval was granted for this study. Informed consent was not required because the data were deidentified before acquisition.

Concussion, Composite Scores, and Symptom Clusters

Concussion was defined according to previously published guidelines for working with ImPACT data. In brief, a significant deviation from baseline in at least 2 of the 5 composite scores was considered a concussion. Significant deviation is defined as a difference greater than the 80% CI of the deviation between 2 baseline tests of healthy control participants (S_{diff}).[24] The composite scores are Verbal Memory ($S_{diff} = 8.75$), Visual Memory ($S_{diff} = 13.55$), Reaction Time ($S_{diff} = 0.06$), Processing Speed ($S_{diff} = 4.98$), and Symptom ($S_{diff} = 9.18$). The Symptom composite score can be broken down into 4 clusters (Migraine, Cognitive, Sleep, and Neuropsychiatric) that categorize the symptoms induced by the injury. These clusters entail the same symptoms as have been previously described.[28,29]

Incidence, SI, and Recovery

Incidence rates were calculated using the number of head traumas or concussions and person-years at risk for injury. Patients required a baseline test to be considered at risk for injury. Person-years were calculated based on time from a participant's baseline test to his or her next baseline or postinjury test. ImPACT baseline tests are reported to be stable for 2 years, so no more than 2 person-years were given for any baseline test. Patients with no further testing after their initial baseline test were considered lost to follow-up.[5,6,42] In accordance with Centers for Disease Control and Prevention guidelines, participants lost to follow-up contributed 1 person-year.[8]

To estimate the severity of each head trauma and/or concussion, we calculated the previously published SI. To calculate SI, each composite score from the postinjury test is compared with the same composite score from the baseline test. If the difference exceeds S_{diff} for that composite score in the adverse direction, then the difference is considered significant and the difference is divided by S_{diff}. The sum of all significant composite score differences standardized by their respective S_{diff} is the SI.[22]

Recovery was assessed using a survival analysis in which the event was defined as recovery from concussion. Recovery from concussion was defined as having 0 or 1 composite scores that remained significantly deviated from baseline at PI2 testing. Kaplan-Meier plots were generated to demonstrate the relative recovery rate between cohorts for 50 days after PI1. Only patients who had a baseline, PI1, and PI2 tests were included. Due to evident demographic differences between cohorts, a Cox proportional hazards regression was used (MatLab; The MathWorks) to control for possible confounders. Potential confounders included in the regression were SI at PI1, age, and binary indicators for diagnosed learning disability (DLD), diagnosis of attention-deficit/hyperactivity disorder (ADHD), history of concussion, and sport (football vs nonfootball).

Statistical Analysis

All other statistical analyses were conducted with Prism 8.0 (GraphPad). Chi-square tests were used to compare incidence rates and differences between categorical variables.[33] Log-rank tests were used to compare Kaplan-Meier curves, and *t* tests were used to compare means of all other analyses. To control for possible demographic confounders, multivariable logistic regression was used to assess differences in incidence between the cohorts. The covariates in this model were age and binary indicators for DLD, ADHD, history of concussion, and sport. The same covariates were included in a multivariable linear regression model assessing the effect of sex on SI. A latency to PI2 logistic regression was performed to evaluate for differences between cohorts in the recovery time elapsed between PI1 and PI2. In this model, SI at PI1 was included as an

TABLE 1
Cohort Characteristics[a]

	Male Participants (n = 7622)	Female Participants (n = 3941)	*P* Value
Age, y, mean ± SD	15.37 ± 1.56	15.33 ± 1.54	.22
Sport: football	4425 (58.1)	120 (3.04)	**<.0001**
Attention-deficit/hyperactivity disorder	439 (5.76)	139 (3.53)	**<.0001**
Diagnosed learning disability	220 (2.89)	102 (2.59)	.36
History of concussion	667 (8.75)	309 (7.84)	.09
Symptom	4.66 (4.47-4.85)	7.48 (7.13-7.84)	**<.0001**
Verbal Memory	81.86 (81.62-82.10)	84.06 (83.68-84.51)	**<.0001**
Visual Memory	72.35 (72.05-72.66)	71.62 (71.08-72.16)	**.02**
Processing Speed	34.52 (34.36-34.69)	36.02 (35.74-36.29)	**<.0001**
Reaction Time	0.639 (0.637-0.642)	0.634 (0.630-0.638)	**.03**

[a]Data are provided as n (%) or mean (95% CI) unless otherwise noted. Boldface *P* values indicate statistical significance.

additional covariate. Finally, a multivariable logistic regression was used to evaluate differences in likelihood that participants remained concussed at PI2 while we controlled for differences in time elapsed between PI1 and PI2. In addition to latency to PI2, all covariates included in the latency to PI2 model were controlled for in this model. For all analyses, $\alpha = .05$.

RESULTS

A total of 7622 male and 3941 female baseline tests were included in the incidence calculations. The age of the male cohort was similar to that of the female cohort (male vs female, 15.37 ± 1.56 vs 15.33 ± 1.54, respectively; $P = .22$). Male participants had a higher percentage of reported ADHD than did female participants (5.76% vs 3.53%; $P < .0001$). There was a large difference in the percentage of athletes who played football (58.1% vs 3.0%; $P < .0001$) as well as significant differences between cohorts in other sports (Appendix Table A1, available in the online version of this article). A full breakdown of sports played by each cohort is provided in Appendix Table A1 (available online). The percentage of athletes with a history of 2 or more previous concussions (8.75% vs 7.84%; $P = .09$) or DLD (2.89% vs 2.59%; $P = .36$) did not differ significantly between male and female athletes. All baseline composite scores differed significantly between male and female participants. Male participants had lower Verbal Memory (81.86 vs 84.06; $P < .0001$), Processing Speed (34.52 vs 36.02; $P < .0001$), and slower Reaction Time (0.639 vs 0.634; $P = .03$), whereas female participants had higher Symptom (4.66 vs 7.48, $P < .0001$) and lower Visual Memory (72.35 vs 71.62; $P = .02$) scores (Table 1).

The incidence of all head traumas per 1000 person-years did not differ between male and female participants (494.2 vs 484.4, respectively; $P = .57$). However, the mean SI of all head traumas was lower for male than female patients (3.39 vs 3.87; $P = .002$). This difference in SI was a result of significant increases in deviation from baseline for Symptom (1.02 vs 1.37; $P < .0001$), Verbal Memory (0.56 vs 0.69; $P < .0001$), and Processing Speed (0.34 vs 0.43; $P = .0008$). There was no significant difference in deviation from baseline for Visual Memory (0.39 vs 0.43; $P = .06$) or Reaction Time (0.96 vs 0.94; $P = .72$) between groups (Table 2).

The unadjusted incidence of concussion per 1000 person-years was also not significantly different between male and female participants (170.0 vs 185.9, respectively; $P = .09$). Nevertheless, a lower percentage of males who experienced a head trauma met concussion criteria (34.4% vs 38.4%; $P = .005$). Females had significantly higher deviations in Processing Speed (0.91 vs 1.06; $P = .01$) and Symptom (2.40 vs 2.94; $P < .0001$) composite scores (Table 2), but the SI for concussion was not different between the male and female participants in unadjusted analyses (8.30 vs 8.67; $P = .21$). However, adjusted analyses controlling for demographic differences showed that female participants had higher concussion incidence (odds ratio, 1.62; 95% CI, 1.40-1.86; $P < .0001$) and higher SI ($\beta = 0.67$; 95% CI, 0.02-1.32; $P = .04$) (Table 3).

Female participants took significantly more time between PI1 and PI2 (male vs female, 9.75 vs 11.77 days, respectively; $P = .01$) (Table 3). There was no difference between male and female groups in the percentage of patients who returned for follow-up (69.1% vs 70.2%; $P = .62$) or in the percentage of patients who remained concussed at PI2 (26.3% vs 26.5%; $P = .95$). Log-rank comparisons of Kaplan-Meier curves demonstrated that female participants recovered significantly slower ($P = .002$) from concussion than male participants. However, when controlling for demographic variables and initial SI with a Cox proportional hazards model, we found no significant effect of sex on time to recovery (hazard ratio, 0.94; 95% CI, 0.78-1.12; $P = .48$) (Figure 1). There was also no significant difference in other recovery indicators such as the odds of remaining concussed at PI2 (odds ratio, 1.21; 95% CI, 0.85-1.73; $P = .29$) or latency to PI2 ($\beta = 0.01$; 95% CI, –1.21 to 1.23; $P = .99$). For patients who remained concussed at PI2, the SI of the concussion was higher in female than in male participants (male vs female, 6.66 vs 8.20, respectively; $P < .001$). This difference was still driven by differences in deviation of Symptom (1.27 vs 1.76; $P < .02$) and Processing Speed (0.68 vs 1.12; $P = .001$) scores (Table 3).

Symptom scores were consistently elevated in female participants. To provide more granularity, the Symptom

TABLE 2
Incidence and Severity Index of All Head Traumas and Concussions[a]

	Male Participants	Female Participants	*P* Value
All head traumas	n = 3465	n = 1751	
Incidence per 1000 patient-years	494.2 (482.5-500.9)	484.4 (468.1-500.7)	.57
Severity Index	3.39 (3.22-3.56)	3.87 (3.61-4.12)	**.002**
Symptom	1.02 (0.96-1.08)	1.37 (1.28-1.47)	<**.0001**
Verbal Memory	0.56 (0.52-0.59)	0.69 (0.63-0.75)	<**.0001**
Visual Memory	0.39 (0.36-0.41)	0.43 (0.39-0.47)	.06
Processing Speed	0.34 (0.31-0.37)	0.43 (0.38-0.48)	**.0008**
Reaction Time	0.96 (0.89-1.03)	0.94 (0.84-1.04)	.72
Concussions	n = 1192	n = 672	
Incidence per 1000 patient-years	170.0 (161.2-178.8)	185.9 (173.2-198.6)	.09
Severity Index	8.30 (7.96-8.64)	8.67 (8.21-9.13)	.21
Symptom	2.40 (2.28-2.52)	2.94 (2.76-3.11)	<**.0001**
Verbal Memory	1.70 (1.61-1.79)	1.61 (1.49-1.73)	.23
Visual Memory	0.95 (0.89-1.02)	0.96 (0.88-1.05)	.86
Processing Speed	0.91 (0.84-0.99)	1.06 (0.96-1.16)	**.01**
Reaction Time	2.33 (2.16-2.51)	2.10 (1.88-2.32)	.12

[a]Values in parentheses are 95% CIs. Boldface *P* values indicate statistical significance.

TABLE 3
Comparisons of Concussion Recovery at Follow-up (PI2) and Multivariable Analysis[a]

	Male Participants	Female Participants	*P* Value
Recovery	n = 824	n = 472	
Patients with PI2, %	69.1	70.2	.62
Patients still concussed at PI2, n (%)	217 (26.3%)	125 (26.5%)	.95
Mean duration between tests, d	9.75 (8.89-10.61)	11.77 (10.41-13.12)	**.01**
Median recovery time, d	8.00	9.00	**.002**
Concussions at PI2, deviations from baseline	n = 217	n = 125	
Mean duration between tests, d	9.22 (7.58-10.86)	11.15 (9.40-12.89)	.13
Severity Index	6.66 (6.00-7.31)	8.20 (7.16-9.23)	**.001**
Symptom	1.27 (1.04-1.49)	1.76 (1.36-2.16)	**.02**
Verbal Memory	1.65 (1.44-1.87)	1.76 (1.50-2.02)	.53
Visual Memory	1.07 (.93-1.21)	1.17 (0.98-1.36)	.38
Processing Speed	0.68 (0.53-0.824)	1.12 (0.88-1.36)	**.001**
Reaction Time	1.99 (1.65-2.33)	2.38 (1.86-2.89)	.20

Multivariable Analysis of Sex on Concussion Incidence, Severity Index, and Recovery

Outcome	Estimate	95% CI	
Concussion incidence[b]	OR = 1.62	(1.40 to 1.86)	<**.0001**
Severity index at PI1[b]	β = 0.67	(0.02 to 1.32)	**.04**
Concussion at PI2[c]	OR = 1.06	(0.73 to 1.55)	.75
Latency to PI2[d]	β = 0.01	(–1.21 to 1.23)	.99

[a]Values in parentheses are 95% CIs unless otherwise noted. Boldface *P* values indicate statistical significance. OR, odds ratio; PI1, initial postinjury test; PI2, second postinjury test.

[b]Covariates: age and binary indicators for diagnosed learning disability, attention-deficit/hyperactivity disorder (ADHD), previous concussion history, and sport (football vs nonfootball).

[c]Covariates: age, concussion Severity Index at PI1, latency to PI2, and binary indicators for diagnosed learning disability, ADHD, previous concussion history, and sport (football vs nonfootball).

[d]Covariates: age, concussion Severity Index at PI1, and binary indicators for diagnosed learning disability, ADHD, previous concussion history, and sport (football vs nonfootball).

score can be broken down into clusters: Migraine, Cognitive, Sleep, and Neuropsychiatric. Differences between the cohorts at both PI1 and PI2 are provided in Table 4. At PI1, the Migraine (male vs female, 10.42 vs 12.58, respectively; $P < .0001$), Cognitive (8.10 vs 9.54; $P < .0001$), and Neuropsychiatric (1.68 vs 2.84; $P < .0001$)

TABLE 4
Symptom Clusters and Individual Symptoms[a]

	PI1			PI2		
	Male (n = 1192)	Female (n = 672)	*P* Value	Male (n = 217)	Female (n = 125)	*P* Value
Migraine	10.42 (9.916 to 10.91)	12.58 (11.87 to 13.29)	**<.0001**	5.04 (4.03 to 6.05)	6.25 (4.60 to 7.89)	.19
Headache	2.47 (2.36 to 2.57)	2.68 (2.54 to 2.82)	**.02**	1.28 (0.04 to 1.54)	1.36 (1.04 to 1.68)	.69
Vomiting	0.16 (0.11 to 0.20)	0.11 (0.06 to 0.15)	.16	–0.005 (–0.07 to 0.06)	0.02 (–0.07 to 0.10)	.71
Nausea	0.882 (0.80 to 0.96)	1.12 (1.00 to 1.25)	**.001**	0.25 (0.12 to 0.39)	0.57 (0.29 to 0.84)	**.02**
Balance problems	1.29 (1.20 to 1.38)	1.33 (1.21 to 1.45)	.59	0.76 (0.57 to 0.96)	0.62 (0.34 to 0.90)	.41
Dizziness	1.53 (1.43 to 1.62)	1.80 (1.66 to 1.93)	**.001**	0.78 (0.58 to 0.98)	0.92 (0.63-1.21)	.42
Sensitivity to light	1.71 (1.61 to 1.82)	2.18 (2.04 to 2.32)	**<.0001**	0.86 (0.65 to 1.07)	1.02 (0.73 to 1.30)	.37
Sensitivity to noise	1.39 (1.29 to 1.49)	1.96 (1.82 to 2.09)	**<.0001**	0.74 (0.56 to 0.92)	1.00 (0.73 to 1.27)	.10
Numbness	0.31 (0.25 to 0.38)	0.40 (0.31 to 0.49)	.12	0.07 (–0.02 to 0.15)	0.19 (0.03 to 0.36)	.15
Visual problems	0.67 (0.59 to 0.75)	1.00 (0.87 to 1.12)	**<.0001**	0.30 (0.14 to 0.47)	0.55 (0.27 to 0.83)	.11
Cognitive	8.10 (7.66 to 8.55)	9.54 (8.94 to 10.15)	**<.0001**	4.05 (3.21 to 4.88)	6.03 (4.56 to 7.50)	**.01**
Fatigue	1.21 (1.11 to 1.31)	1.45 (1.30 to 1.60)	**.007**	0.35 (0.17 to 0.53)	0.82 (0.50 to 1.14)	**.006**
Drowsiness	1.41 (1.31 to 1.51)	1.65 (1.51 to 1.79)	**.005**	0.45 (0.27 to 0.63)	0.81 (0.46 to 1.15)	**.048**
Feeling slowed down	1.25 (1.16 to 1.35)	1.60 (1.47 to 1.73)	**<.0001**	0.55 (0.38 to 0.72)	1.05 (0.78 to 1.32)	**.001**
Fogginess	1.49 (1.39 to 1.59)	1.75 (1.61 to 1.88)	**.002**	0.80 (0.61 to 0.99)	0.98 (0.70 to 1.27)	.27
Difficulty concentrating	1.69 (1.58 to 1.80)	2.06 (1.92 to 2.21)	**<.0001**	1.10 (0.87 to 1.33)	1.36 (1.03 to 1.69)	.19
Memory problems	1.05 (0.95 to 1.14)	1.03 (0.90 to 1.16)	.82	0.79 (0.59 to 0.99)	1.01 (0.69 to 1.32)	.23
Sleep	1.73 (1.53 to 1.93)	1.75 (1.47 to 2.03)	.90	0.79 (0.36 to 1.23)	0.99 (0.25 to 1.73)	.62
Difficulty falling asleep	0.75 (0.65 to 0.85)	0.80 (0.65 to 0.95)	.57	0.39 (0.15 to 0.62)	0.46 (0.12 to 0.79)	.73
Sleeping more	0.60 (0.51 to 0.69)	0.78 (0.65 to 0.91)	**.019**	0.20 (0.06 to 0.35)	0.46 (0.18 to 0.75)	.08
Sleeping less	0.38 (0.28 to 0.48)	0.17 (0.02 to 0.31)	**.015**	0.20 (–0.02 to 0.43)	0.07 (–0.28 to 0.43)	.52
Neuropsychiatric	1.68 (1.45 to 1.91)	2.84 (2.43 to 3.25)	**<.0001**	0.60 (0.18 to 1.02)	1.70 (0.75 to 2.66)	**.02**
Irritability	0.83 (0.73 to 0.92)	1.10 (0.96 to 1.23)	**.001**	0.48 (0.29 to 0.67)	0.58 (0.28 to 0.87)	.57
Nervousness	0.27 (0.19 to 0.35)	0.43 (0.29 to 0.56)	**.03**	–0.02 (–0.18 to 0.14)	0.16 (–0.13 to 0.45)	.23
Sadness	0.26 (0.20 to 0.33)	0.59 (0.47 to 0.71)	**<.0001**	0.06 (–0.06 to 0.19)	0.44 (0.17 to 0.70)	**.005**
Feeling more emotional	0.33 (0.26 to 0.40)	0.72 (0.59 to 0.86)	**<.0001**	0.08 (–0.03 to 0.19)	0.53 (0.23 to 0.83)	**.001**

[a]Values are expressed as increase from baseline (95% CI). Boldface *P* values indicate statistical significance. PI1, initial postinjury test; PI2, second postinjury test.

clusters were all significantly higher relative to baseline for female participants. The Sleep cluster (1.73 vs 1.75; *P* = .90) did not differ between male and female participants. Headache and sensitivity to light were the most commonly reported symptoms in both groups. The most seldomly reported symptom was vomiting. Symptoms with significant differences in deviations from baseline between male and female participants are highlighted in Appendix Figure A1 (available online). There were no sex differences for vomiting, balance problems, numbness, difficulty remembering, or difficulty falling asleep.

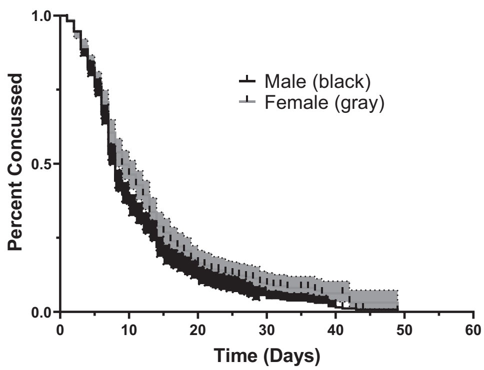
At PI2, female participants reported higher deviations from baseline in both the Cognitive (male vs female, 4.05 vs 6.03, respectively; *P* = .01) and Neuropsychiatric (0.60 vs 1.70; *P* = .02) Symptom clusters. The symptoms that persisted to a greater extent in female than male participants through their first follow-up test were nausea (0.25 vs 0.57; *P* = .02), fatigue (0.35 vs 0.82; *P* = .006), drowsiness (0.45 vs 0.81; *P* = .048), feeling slowed down (0.55 vs 1.05; *P* = .001), sadness (0.06 vs 0.44; *P* = .005), and feeling more emotional than usual (0.08 vs 0.53; *P* = .001). The most common symptoms for both male and female participants were headache (1.28 vs 1.36; *P* = .69) and difficulty concentrating (1.10 vs 1.36; *P* = .19), but there was no sex disparity for these symptoms (Table 4).

DISCUSSION

The present study investigated sex differences in concussion incidence, SI, and recovery in a large, heterogeneous sample of young athletes. Although univariate analysis did not show significant differences, multivariable analyses revealed that female participants had higher incidence and SI of concussion. Initial analyses suggested that female participants took longer to recover from concussion, but subsequent adjusted analyses illustrated that this difference is more likely the result of higher initial concussion SI than sex. Overall, these results were consistent with the current literature on concussion incidence rates in female participants and provide important insight into the mixed results in the current literature surrounding sex differences in concussion recovery. This is the first study to investigate sex differences in concussion severity using the quantitative SI.

Incidence

Concussion incidence was significantly higher in female participants. This is consistent with numerous previous studies.[14,20,30,32,38] Although this finding is pervasive in the literature, explanations for this phenomenon are lacking. One hypothesis is that female patients are more likely



Cox Proportional Hazard Regression	Estimate	95% CI	p-value
Unadjusted	HR = .80	.70 to .92	**.001**
Multivariable[a]	HR = .94	.78 - 1.12	.48

Figure 1. Kaplan-Meier curves showing the rate of recovery from concussion for male and female participants. Log-rank test showed that female participants took a significantly longer time to recover (*P* = .021). However, multivariable Cox proportional hazards modeling demonstrated no effect of sex on time to recovery. Shaded regions represent 95% CIs. Vertical markings indicate censored data of patients lost to follow-up before recovery. Boldface *P* value indicates statistical significance. HR, hazard ratio.
[a]Covariates: age, concussion Severity Index at initial post injury test, latency to second post injury test, and binary indicators for diagnosed learning disability, attention-deficit/hyperactivity disorder, previous concussion history, and sport (football versus non-football).

to report concussion symptoms than their male counterparts.[3,14,35] Consistent with this theory, female participants had higher Symptom composite scores at baseline and still reported larger deviations from baseline in total reported symptoms. However, ImPACT results also showed persistent deficits in the Processing Speed tests in the objective portion of the neurocognitive assessment, indicating that increased incidence is not solely an artifact of increased symptom reporting. It has also been shown that patients with previous concussion history have a lower severity threshold for reporting symptoms, which can artificially exacerbate an incidence disparity.[17] However, in the present study, female participants had higher SI for concussions, suggesting that a lower threshold phenomenon is not responsible for the incidence effect. Other hypotheses for the increased incidence of concussion in female athletes include anatomic, hormonal, and demyelination sex differences; unfortunately, these theories could not be assessed in the present study.[9,40,46] As female participation in sports continues to increase, sex-based considerations for managing concussion risk may be necessary to prevent further widening of this gap.

Severity Index

Female participants had significantly higher SI compared with male participants. This increase was also clinically significant because it led to longer recovery time in unadjusted analyses. The use of the SI may permit a more complete assessment of severity than previously possible because the SI can better delineate severity from recovery time while also predicting recovery.[22] This is the first study to use SI to quantify neurocognitive concussion severity in a prospective fashion, although multiple previous concussion studies have made severity estimations using only Symptom scores or using recovery length as a retrospective indicator.[4,23,27,45,50] These differences in method make comparisons between these previous studies and ours more suited to discussions of symptom clusters and recovery findings rather than severity. However, one study used a method similar to that of the present study and found that deficits in computerized neurocognitive testing were higher in female participants after mTBI.[7] Importantly, those authors also reported higher incidence and symptom burden in female participants. The consistency of these results with those of the present study provides strong evidence that women and girls experience significantly higher severity concussions across multiple dimensions. Significant innovation over current treatments for acute phase mTBI would likely be required to reduce the sex differences of initial SI reported here. However, these results do suggest heightened attention to symptom management might benefit female athletes who experience mTBI.

Upon further examination of the increased SI in the female cohort, we identified Symptom and Processing Speed composite scores as the significant factors producing the difference in overall SI (Table 2; Appendix Table A2, available online). Other studies have investigated sex differences in the various ImPACT composite scores, finding widely varying results.[10,15,19,31] One study found a significant effect on Processing Speed, but no effect on Symptom scores, whereas another found no effect on Processing Speed but a significant effect on Symptom score.[10,31] Most of these studies had <100 participants and 1 had as few as 13 female participants. Thus, although our study adds to an already convoluted picture, it may be a more accurate depiction of the sex differences in neurocognitive presentation of acute mTBI due to the large increase in sample size compared with previous work. Moreover, the results of the neurocognitive test appear to align with the reported symptoms. For example, female participants had larger deficits in Processing Speed and reported feeling slowed down more often than did male participants. Additionally, female patients demonstrated no differences in Verbal or Visual Memory compared with male patients and did not report increased memory problems in the Symptom score. So, although the results presented here cannot be corroborated by the heterogeneous results present in the current literature, the subjective symptoms mirroring the objective cognitive testing provide support for their validity. Furthermore, recent imaging studies provide further evidence to substantiate our findings. Specifically, one study showed that after mTBI, male (compared with female) patients had significantly increased connectivity in the ventral stream network known to play an integral role in visual processing; another study linked increased thickness of the left caudal anterior cingulate cortex to increased Symptom scores in female patients compared with male patients after mTBI.[43,48]

Previous studies have examined symptom cluster discrepancies between the sexes in amateur athletes both at baseline and after concussion.[12,13,16,39,50] Although these studies agree that female athletes experience more symptoms than male athletes, the specific clusters that differ between the sexes has been inconsistent, due in part to inconsistent methods. The current study found significant discrepancies between male and female participants in Migraine, Cognitive, and Neuropsychiatric clusters in the acute phase and differences in Cognitive and Neuropsychiatric clusters at follow-up. Cognitive and Migraine cluster symptoms are the classic symptoms of concussion, whereas Neuropsychiatric symptoms are less traditional but often have an insidious effect on recovery and daily living.[41] The Neuropsychiatric cluster consists of irritability, nervousness, sadness, and feeling more emotional than usual. The literature on neuropsychiatric outcomes after concussion is mixed.[12,25,39,47,49] Some studies show that female patients experience more affective symptoms after traumatic brain injury.[39,49] However, other studies have found no difference in affective symptoms between male and female participants after mTBI.[12,25,47,50] The current study provides evidence that female patients are at higher risk of mood disturbances after mTBI. Therefore, heightened vigilance for these symptoms is appropriate when monitoring recovery from mTBI in female athletes. Additionally, pharmacotherapies may have a role in reducing sex differences of acute concussion severity.[44]

Recovery

Sex differences specific to concussion recovery length have been previously studied and, like symptom cluster profiles, the results have been mixed. Some studies found no significant difference.[11,21,36,39,50] Others found that female participants experienced protracted recovery compared with male participants.[18,34,50] The results of the present study may provide some nuance. Univariate analyses demonstrated that female participants had longer median recovery compared with male participants; however, this effect dissipated when controlling for initial SI. This indicates that female patients recover at the same rate as their male counterparts, but female patients are recovering from more severe concussions. Because many of the previous studies did not control for initial severity or quantified severity based solely on Symptom scores, this putative effect may have been overlooked. Importantly, however, for female participants who were still concussed at follow-up, the SI gap between male and female participants increased, suggesting that there may be sex differences in recovery for the most severe concussions. This is an important future investigation.

Limitations

This study is limited by its retrospective nature. Specifically, it is unclear how long patients participated in athletics after their baseline test. Recovery length in this study is likely an overestimation because patients could have recovered any day before PI2. ImPACT is an imperfect measure of concussion and is susceptible to false-positive and false-negative results. The recovery analyses in this study are not robust to symptom relapse during return-to-play protocols. Furthermore, it is not known how long it took patients to recover if they still had a concussion at PI2, because this was the primary endpoint. Finally, the age range of these participants covers an important developmental period, and previous research has shown an interaction between age and sex for some symptoms within the post-concussion symptom scale. Although we controlled for age in our regression analyses, we did not investigate the interaction between age and sex on concussion outcomes during adolescent development.[13]

CONCLUSION

This study investigated differences between young male and female athletes for the incidence, SI, and recovery of concussion. Multivariable analysis demonstrated that female participants had increased concussion incidence and higher scores on the SI. No effect of sex was observed on recovery when accounting for initial SI. Differences in SI were the result of significant differences in Symptom and Processing Speed composite scores. Female participants had significantly higher Migraine, Cognitive, and Neuropsychiatric symptom cluster scores at their initial postinjury ImPACT test. With a large, diverse sample, this study provides generalizable evidence that female participants are at higher risk for concussion and that these concussions are more severe. As female participation in high-risk sports continues to increase, these disparities are likely to increase without targeted risk mitigation.

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