Quantifying the value of multidimensional assessment models for acute concussion: an analysis of data from the NCAA-DoD Care Consortium

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Abstract

Background

Many concussion assessment methods exist, but few studies quantify the performance of these methods to determine which can best assess acute concussion alone or in combination.

Objectives

Evaluate: (1) selected concussion assessments for acute concussion assessment; (2) the utility of change scores for acute concussion assessment; (3) concussion assessment capabilities when constrained to limited clinical data or objective clinical measures.

Methods

The "acute concussion" group contained assessments from <6 hours post-injury (n=560) and 24-48 hours post-injury (n=733). The "normal performance" group contained assessments from baseline testing (n=842) and unrestricted return to play (n=707) timepoints. Univariate and multivariate logistic regression models were created separately for <6 hours and 24-48 hours timepoints. Models were evaluated on sensitivity, specificity, and area under the curve (AUC).

Results

Within univariate analysis, SCAT symptom assessments had the highest combination of sensitivity, specificity, and AUC, with values up to 0.93, 0.97, and 0.98, respectively. Full models had a sensitivity, specificity, and AUC up to 0.94, 0.97, and 0.99, respectively, and outperformed all univariate models, raw score models, and objective models. Objective models were outperformed by all multivariate models and the univariate models containing only SCAT symptom assessments.

Conclusion

Results support the use of multidimensional assessment batteries over single instruments and suggest the importance of self-reported symptoms in acute concussion assessment. Balance assessments, however, may not provide additional benefit when symptom and neurocognitive assessments are available.

Additionally, change scores provide some clinical utility over raw scores, but the difference may not be clinically meaningful.

Key Points

- Multivariate logistic regression models which combine multiple assessments, injury characteristics, and individual risk modifiers are sensitive to the effects of acute concussion and can provide a single measure to guide the assessment of acute concussion.
- Self-reported symptoms play a significant role in the assessment of acute concussion; omitting symptoms from multidimensional assessment models resulted in the greatest decrease in discrimination ability.
- While incorporating baseline assessment information in multidimensional assessment models improved each models' discrimination ability, acute concussion assessment may still be performed at clinically acceptable levels of accuracy when baseline information is unavailable.

1 INTRODUCTION

Concussion is an emerging public health issue [1]. For athletes in the National Collegiate Athletic Association (NCAA), concussion occurs at an overall incidence rate of 4.47 per 10,000 Athlete-Exposures, though incidence rates differ greatly by sport [2]. Concussion is characterized by the alteration of neurologic function and development of wide-ranging symptoms including confusion, memory-loss, and headaches [1,3–5]. Recent studies suggest links between concussions and long-term consequences such as physical and cognitive impairment, psychological health problems (e.g., depression), and neurodegenerative disease, including Chronic Traumatic Encephalopathy (CTE) [6–12]. To mitigate the effects of these consequences, numerous efforts have been launched to determine best practices in concussion management.

In sporting environments, concussion diagnosis is critical for proper injury management and must be both timely and accurate. To this end, many challenges remain for physicians and athletic trainers. One major challenge lies in the simultaneous use and interpretation of various concussion assessment tools. Multiple domestic and international organizations recommend clinicians implement multiple tests to evaluate several domains to support the clinical examination of the injured athlete [1,3–5]. Commonly used assessments include the Standard Assessment of Concussion (SAC), athlete-reported symptoms, and the Balance Error Scoring System (BESS). Unfortunately, few studies have quantified the performance of these methods to determine which are most accurate in identifying concussions alone or in combination. Among the studies which have analyzed these assessments for the evaluation of concussion, many of them consider only one assessment in isolation [13–17]. Moreover, most of these studies analyzed a small sample of male football athletes who have experienced concussion, limiting the generalizability of the results across sexes and sports. Additionally, while it is widely accepted that combining multiple assessments (i.e., a testing battery such as the Sport Concussion Assessment Tool 5th Edition (SCAT5) [18]) improves concussion assessment capability [1,4,5], no method combines the results of multiple tests into a single measure for guiding injury assessment – making the simultaneous interpretation of test results difficult. Another challenge in acute concussion assessment lies in the importance of change scores, i.e., the differences between an athlete's performance prior to and following injury. While many assessment methods require the use of change scores, these data may not always be available to clinicians and when they are, their utility has been questioned [19–21]. Similarly, another challenge lies in determining which clinical measures can be used for concussion assessment when data is unavailable or when self-reported symptoms are unreliable. Finally, while a number of modifying factors (e.g., age[22–24], sex[22,24–27], and concussion history[27–30]) have been suggested to influence concussion risk and affect injury presentation, how to incorporate these risk modifiers in acute concussion assessment remains unclear.

The goal of this study is to address these aforementioned challenges in acute concussion assessment through a statistical modeling approach. Specifically, this study aims to: (1) evaluate selected standard assessments for the evaluation of acute concussion; (2) determine the assessments for which change score has more clinical utility than raw score for evaluating acute concussion; (3) quantitatively evaluate concussion assessment under limited clinical data or objective clinical measures. These aims are achieved by building, analyzing, and validating logistic regression models using data from a nationwide and multi-site study on sports-related concussions. This approach not only provides insight into which combinations of standard assessments are most important in acute concussion assessment, but it also combines these measures into a single risk estimate which can be used to guide clinical decision-making in the evaluation of acute concussion.

2 METHODS

2.1 Study design and participants

The deidentified data used in this secondary analysis was provided by the Concussion Assessment, Research, and Education (CARE) Consortium [31]. Throughout the CARE Consortium, concussion is defined from evidence-based guidelines as “a change in brain function following a force to the head, which may be accompanied by temporary loss of consciousness, but is identified in awake individuals with measures of neurologic and cognitive dysfunction” [32]. This data, consisting of 22,057 player-seasons, was collected during the 2014-2017 academic years from 29 National College Athletic Association (NCAA) universities and military service academies. Most player-seasons were for football (22.40%), cross country/track (12.1%), and soccer (11.2%). This data included 16,142 participants who completed a pre-season baseline assessment. There were 941 concussions recorded among 870 athletes. Athletes diagnosed with a concussion were evaluated at the time of injury (<6 hours), 24-48 hours post-injury (24-48 hours), when he/she identified as asymptomatic, when cleared for unrestricted return-to-play (RTP), and 6 months after unrestricted RTP. All concussion diagnoses were made by the local institution’s medical staff (e.g., team physicians and athletic trainers) and all participants provided written informed consent that was approved by their local institution and the US Army Human Research Protection Office (HRPO). This study was conducted in accordance with the standards of ethics outlined in the Declaration of Helsinki.

2.2 Measures

The timepoints considered in this study included baseline assessments and post-injury assessments from <6 hours, 24-48 hours, and at the time of unrestricted RTP. Concussions without a baseline assessment prior to the injury were excluded from the analysis (n=62). Variables in this study include concussion risk modifiers (e.g., age and sex), the SAC, the Standard Concussion Assessment Tool

(SCAT) symptom evaluations, and the BESS. The risk modifiers selected for this study have been previously identified as potential indicators for increased risk of concussion. Similarly, the selected assessments have been identified as practical and effective methods for evaluating concussion [1,4,33]. Furthermore, the individual assessments considered in this study are also part of existing, widely-used, and easily available testing batteries such as the SCAT5. Finally, as a clinical benefit, these study variables can also be obtained within the time constraints of athletics – making them useful for sideline assessment. For the SAC, SCAT symptom evaluations, and BESS, both raw score and change score were considered. Change score for a timepoint is defined as the difference between the raw score at that timepoint and the raw score at baseline. That is, a positive change score implies that an athlete scored higher post-injury compared to baseline and a negative change score implies that an athlete scored lower post-injury compared to baseline. The variables considered in this analysis are described in more detail below.

2.2.1 Concussion Risk Modifiers

Select variables thought to influence concussion risk were selected for modeling. Younger athletes, females, and those with previous concussions may be at higher risk for concussion [1,4,5,8]. Additionally, injury characteristics such as whether the athlete experienced loss of consciousness (LOC), post-traumatic amnesia (PTA), and retrograde amnesia (RGA) are associated with concussion [1,4,5]. Whether the athlete was removed from play immediately and reported the injury immediately can modify the symptom presentation at the time of assessment [1,4,5,34,35].

2.2.2 Standard Assessment of Concussion

The SAC is an instrument which includes measures of orientation, immediate memory, concentration, and delayed recall [36]. The SAC total score is considered to provide a holistic measure of neurological status, so the SAC total score and change score were considered in this study.

2.2.3 Sports Concussion Assessment Tool Symptom Evaluations

The SCAT symptom list is a standardized tool for evaluating symptom presentation among injured athletes [37]. Hence, the total number of symptoms reported and the total symptom severity score were included as variables, along with their change scores.

2.2.4 Balance Error Scoring System

The BESS is a physical examination consisting of a double-leg stance, single-leg stance, and a tandem stance [38]. Since impaired balance is believed to indicate concussion, the BESS total score and change score were considered.

2.3 Data analysis

Most study variables were missing at <6% across all timepoints. The BESS assessments were missing at <10% for all timepoints except <6 hours, which was missing at 26.61%. Multiple imputation by chained equations was used to fill missing data [39]. This method is common in medical literature, including previous concussion studies [17,40,41]. Imputation was performed using the software R version 3.2.2.

2.4 Quantifying the difference between acute concussion and normal performance

The probability of belonging to the “acute concussion” group was estimated using logistic regression. The “acute concussion” group consisted of post-injury assessments from <6 hours or 24-48 hours and the “normal performance” group consisted of assessments from baseline and unrestricted RTP. Separate models were created for the <6 hours and 24-48 hours timepoints. For the baseline data, it was assumed that all change scores were 0, the injury was reported immediately, the athlete was removed from play immediately, and the athlete did not experience LOC, PTA, or RGA. These assumptions were made since these variables were not measured during baseline evaluations and values were needed for logistic regression. To perform the analysis, all data, excluding baseline data, were randomly split into training (75%) and testing (25%) sets. Baseline data were excluded from the training set to prevent model fitting from being influenced by baseline data assumptions. Five-fold cross-validation was performed on the training set to select and parameterize the models. Models were first validated using the testing set, which consisted of data from the unrestricted RTP group and the appropriate acute concussion group. Then, baseline data were used to validate the models separately.

Univariate logistic regression analysis was performed to understand how each study variable, individually, is associated with acute concussion. Then, multivariate logistic regression was performed using backward variable selection with Akaike Information Criteria [42]. The goal of the multivariate logistic regression was to understand how the study variables, in combination, are associated with acute concussion (*full models)*. If the resulting variables contained both change score and raw score for the SAC, SCAT symptom assessments, or BESS, then two models were created for each instance. One model contained all variables resulting from backward variable selection except change score for that assessment and the other model contained all variables except raw score. The model with better performance measures on the training set was kept.

To assess multivariate model performance under limited data, full models were modified to estimate the impact of deleting one variable (*limited models*). These limited models highlight which variables most drastically affect the full model's performance when certain measures are unavailable. To create limited models, the full model was recreated on the training set with all variables except one. This procedure was repeated until a limited model was created for every variable in the full model.

The impact on concussion assessment when baseline data is unavailable was evaluated by creating models which replaced all change score assessments in the full model with raw scores (*raw score models*).

Finally, since symptom under-reporting is a major concern within concussion management [43], multivariate models were created to estimate model performance without self-reported symptoms (*objective models*). Objective models were created using the same procedure as the full model except SCAT total symptoms and SCAT symptom severity were excluded from the initial set of variables. Models were created and analyzed using Python 3.5.2.

2.5 Performance Measures

Models were evaluated on sensitivity, specificity, and area under the curve (AUC). Sensitivity is the percentage of acute concussions at <6 hours or 24-48 hours correctly classified as acute concussions and specificity is the percentage of normal performance assessments from the baseline or unrestricted RTP timepoints correctly classified as normal performance. AUC is the likelihood that a model will estimate the probability of acute concussion to be higher for a randomly chosen acute concussion than a randomly chosen normal performance. Additionally, the limited models, raw score models, and objective models were compared to the full models using a bootstrap test for AUC on the testing set (*bootstrap test*) [44]. A significant p-value suggests that a given model's AUC is less than the full model's.

3 RESULTS

The study data with respect to selected concussion risk modifiers and standard assessments are summarized in Table 1. The groups do not differ significantly in terms of height, weight, age, sex, and previous number of concussions. However, the raw scores for the groups at <6 hours, 24-48 hours, and unrestricted RTP differ significantly from the baseline group (p-value <0.01).

Table 1: Characteristics of the study data with reference to selected variables by timepoint

Variable	Baseline	<6 hours	24-48 hours	Unrestricted RTP
n*	842	560	733	707
Days since injury (SD)*	NA	0.39 (7.66)	0.92 (1.80)	14.47 (12.66)

Height in meters (SD)*	1.80 (0.12)	1.80 (0.10)	1.79 (0.12)	1.79 (0.12)
Weight in kg (SD)*	84.04 (21.77)	86.24 (22.80)	83.68 (21.93)	83.22 (21.57)
Age in years (SD)	19.40 (1.30)	19.37 (1.31)	19.33 (1.27)	19.37 (1.30)
Male Sex (% yes)	61.52%	64.46%	60.03%	59.83%
Number of previous concussions (SD)	0.75 (1.02)	0.79 (1.04)	0.75 (1.05)	0.71 (0.95)
Report injury immediately? (% yes)	NA	53.57%	39.29%	39.75%
Removed from play immediately? (% yes)	NA	56.07%	45.98%	47.52%
LOC? (% yes)	NA	5.71%	4.50%	5.23%
PTA? (% yes)	NA	11.79%	11.19%	11.32%
RGA? (% yes)	NA	5.89%	6.14%	5.94%
SAC change score (SD)	NA	-0.83 (3.19)	-0.42 (2.60)	0.96 (2.13)
SAC raw score (SD)	27.05 (2.01)	26.18 (2.92)**	26.61 (2.42)**	27.93 (1.75)**
SCAT symptom severity change score (SD)	NA	23.47 (20.90)	19.53 (21.87)	-4.92 (8.81)
SCAT symptom severity raw score (SD)	5.08 (8.44)	28.79 (20.87)**	25.16 (21.64)**	0.63 (1.99)**
SCAT total symptoms change score (SD)	NA	8.07 (5.96)	7.48 (6.59)	-2.51 (4.02)
SCAT total symptoms raw score (SD)	2.77 (3.82)	10.89 (5.42)**	10.49 (6.02)**	0.47 (1.40)**
BESS change score (SD)	NA	3.68 (8.66)	1.43 (7.42)	-2.31 (6.27)
BESS raw score (SD)	12.62 (6.29)	16.41 (8.74)**	14.32 (7.87)**	10.40 (5.76)**

n, number of data points
SD, standard deviation
NA implies that the measure was not taken at baseline
Change score at a timepoint is computed as: raw score at timepoint - raw score at baseline
*variable was not considered in the models
**p-value < 0.01 when compared to mean value at baseline using t-test

3.1 Univariate logistic regression analysis

The relationships between individual variables and acute concussion are summarized in Table 2. These results address aim (1). For both <6 hours and 24-48 hours models, the SAC, SCAT symptom assessment, and BESS had significant p-values (<0.05). In contrast, age and sex both had p-values which were not significant (>0.05). Within the 24-48 hours univariate analysis, the variables PTA, RGA, and LOC had negative coefficients suggesting that these factors reduce one's likelihood of having acute concussion when present. This contradictory finding may be due to variance in the estimates; their p-values suggest that their coefficients are not significantly different from 0. To avoid implications that PTA, RGA, and LOC are "protective", these variables were removed from multivariate analysis. The performance measures for all univariate models are available in Electronic Supplementary Material Appendix S1. These results address aim (2). For both <6 hours and 24-48 hours models, raw scores for SCAT symptom severity and SCAT total number of symptoms resulted in the greatest combination of AUC and sensitivity. For the SAC and BESS, the raw score univariate models performed similarly to their change score counterparts.

Table 2: Results of the univariate logistic regression for association between risk factors and concussion for <6 hours and 24-48 hours

Variable	**<6 hours**			**24-48 hours**		
	Intercept (SE)	*Coefficient (SE)*	*p-value*	*Intercept (SE)*	*Coefficient (SE)*	*p-value*
Age in years	-1.46 (0.98)	0.07 (0.05)	0.19	0.11 (0.91)	0.00 (0.05)	0.96
Male Sex	-0.31 (0.11)	0.22 (0.14)	0.11	0.11 (0.10)	-0.06 (0.13)	0.61
Number of previous concussions	-0.24 (0.08)	0.10 (0.07)	0.14	0.04 (0.08)	0.04 (0.06)	0.56
Report injury immediately?	-0.36 (0.09)	0.41 (0.13)	0.00	0.07 (0.08)	0.00 (0.13)	0.97
Removed from play immediately?	-0.36 (0.10)	0.36 (0.13)	0.01	0.09 (0.08)	-0.03 (0.12)	0.78
LOC?	-0.18 (0.07)	0.14 (0.28)	0.62	0.08 (0.06)	-0.12 (0.29)	0.69
PTA?	-0.20 (0.07)	0.25 (0.20)	0.21	0.08 (0.06)	-0.06 (0.19)	0.76
RGA?	-0.17 (0.07)	-0.04 (0.27)	0.88	0.08 (0.06)	-0.17 (0.26)	0.50
Number of hours of sleep last night?	-0.37 (0.33)	0.03 (0.04)	0.54	-1.16 (0.28)	0.16 (0.04)	0.00
SAC change score	-0.12 (0.07)	-0.25 (0.03)	0.00	0.13 (0.06)	-0.25 (0.03)	0.00
SAC raw score	8.90 (0.93)	-0.33 (0.03)	0.00	8.76 (0.92)	-0.32 (0.03)	0.00
SCAT symptom severity change score	-1.17 (0.11)	0.27 (0.02)	0.00	-0.59 (0.09)	0.20 (0.01)	0.00
SCAT symptom severity raw score	-3.19 (0.21)	0.58 (0.04)	0.00	-2.18 (0.14)	0.50 (0.04)	0.00
SCAT total symptoms change score	-1.16 (0.12)	0.60 (0.04)	0.00	-0.67 (0.09)	0.46 (0.03)	0.00
SCAT total symptoms raw score	-3.30 (0.22)	0.94 (0.07)	0.00	-2.32 (0.15)	0.76 (0.05)	0.00
BESS change score	-0.23 (0.07)	0.12 (0.01)	0.00	0.10 (0.06)	0.09 (0.01)	0.00
BESS raw score	-1.70 (0.16)	0.12 (0.01)	0.00	-0.98 (0.14)	0.09 (0.01)	0.00

SE, standard error
Change score at a timepoint is computed as: raw score at timepoint - raw score at baseline

3.2 Multivariate logistic regression analysis

Final variables in each full model are summarized in Table 3. These results address aims (1). Both full models contained sex, whether the injury was reported immediately, SAC change score, SCAT symptom severity change score, and SCAT total symptoms raw score. The <6 hours model contained BESS change score while the 24-48 hours model contained BESS raw score. Every variable in the full model was significant except for whether the athlete was removed from play immediately in the <6 hours model and the BESS raw score in the 24-48 hours model.

Table 3: Factors in multivariate logistic regression (full model) associated with acute concussion at <6 hours and 24-48 hours

Variable	**<6 hours**		**24-48 hours**	
	Coefficient (SE)	*p-value*	*Coefficient (SE)*	*p-value*
Intercept	-4.51 (0.53)	0.00	-2.67 (0.35)	0.00
Male Sex	1.02 (0.42)	0.01	0.56 (0.26)	0.03
Report injury immediately?	1.85 (0.44)	0.00	0.74 (0.24)	0.00
Removed from play immediately?	-0.64 (0.41)	0.12	NA	NA
SAC change score	-0.16 (0.08)	0.04	-0.13 (0.05)	0.01
SCAT symptom severity change score	0.13 (0.03)	0.00	0.07 (0.02)	0.00
SCAT total symptoms raw score	1.01 (0.09)	0.00	0.73 (0.06)	0.00
BESS change score	0.09 (0.03)	0.00	NA	NA
BESS raw score	NA	NA	-0.01 (0.02)	0.73

SE, standard error
Change score at a timepoint is computed as: raw score at timepoint - raw score at baseline
NA implies that the variable was not included in the model

The sensitivity, specificity, and AUC for all multivariate models are summarized in Table 4 and Receiver Operating Characteristic (ROC) curves for selected models are shown in Figure 1. These results address aims (2) and (3). Full models outperformed all univariate models. The coefficients for the limited models, raw score models, and objective models are presented in Electronic Supplementary Material Appendix S2. At <6 hours and 24-48 hours, removing SCAT total symptoms raw score from the full model resulted in the greatest decrease in performance. At <6 hours, removing whether the injury was reported immediately, whether the athlete was removed from play immediately, or the BESS change score from the full model does not reduce AUC significantly (p-value>0.10). Similarly, removing BESS raw score from the full model at 24-48 hours does not reduce AUC significantly. Full models achieved greater AUC than raw score models (p-value<0.001).

Table 4: Testing set and training set estimates for performance measures of multivariate models at <6 hours and 24-48 hours

Model	**<6 hours**			**24-48 hours**		
	Sensitivity	*Specificity**	*AUC*	*Sensitivity*	*Specificity**	*AUC*
Full model	0.93 (0.94)	0.96 (0.97)	0.98 (0.99)	0.85 (0.88)	0.97 (0.96)	0.97 (0.97)
Limited models Full (-removed variable)						
Full (-Male Sex)[1,2]	0.92 (0.94)	0.95 (0.97)	0.98 (0.99)	0.86 (0.88)	0.96 (0.95)	0.97 (0.96)
Full (-Report injury immediately?)[2]	0.92 (0.93)	0.96 (0.97)	0.98 (0.99)	0.86 (0.88)	0.97 (0.95)	0.97 (0.96)
Full (-Removed from play immediately?)	0.92 (0.93)	0.96 (0.97)	0.98 (0.99)	NA	NA	NA
Full (-SAC change score)[1]	0.93 (0.93)	0.96 (0.97)	0.98 (0.99)	0.84 (0.89)	0.96 (0.95)	0.97 (0.96)
Full (-SCAT symptom severity change score)[1,2]	0.91 (0.92)	0.96 (0.97)	0.97 (0.99)	0.85 (0.88)	0.95 (0.95)	0.96 (0.96)
Full (-SCAT total symptoms raw score)[1,2]	0.86 (0.88)	0.96 (0.97)	0.96 (0.95)	0.75 (0.81)	0.96 (0.94)	0.93 (0.91)
Full (-BESS change score)	0.93 (0.93)	0.95 (0.98)	0.98 (0.99)	NA	NA	NA
Full (-BESS raw score)	NA	NA	NA	0.84 (0.88)	0.97 (0.96)	0.97 (0.97)
Raw score model[1,2]	0.92 (0.93)	0.96 (0.97)	0.98 (0.98)	0.84 (0.87)	0.95 (0.95)	0.97 (0.96)
Objective model[1,2]	0.61 (0.60)	0.74 (0.81)	0.73 (0.76)	0.60 (0.66)	0.70 (0.68)	0.68 (0.72)

All values are reported as: testing set estimate without baselines (training set estimate)
Change score at a timepoint is computed as: raw score at timepoint - raw score at baseline
NA implies that the variable was not included in the model
[1]p-value < 0.001 in bootstrap test for AUC, <6 hours
[2]p-value < 0.001 in bootstrap test for AUC, 24-48 hours
*Specificity estimates do not include the baseline data.

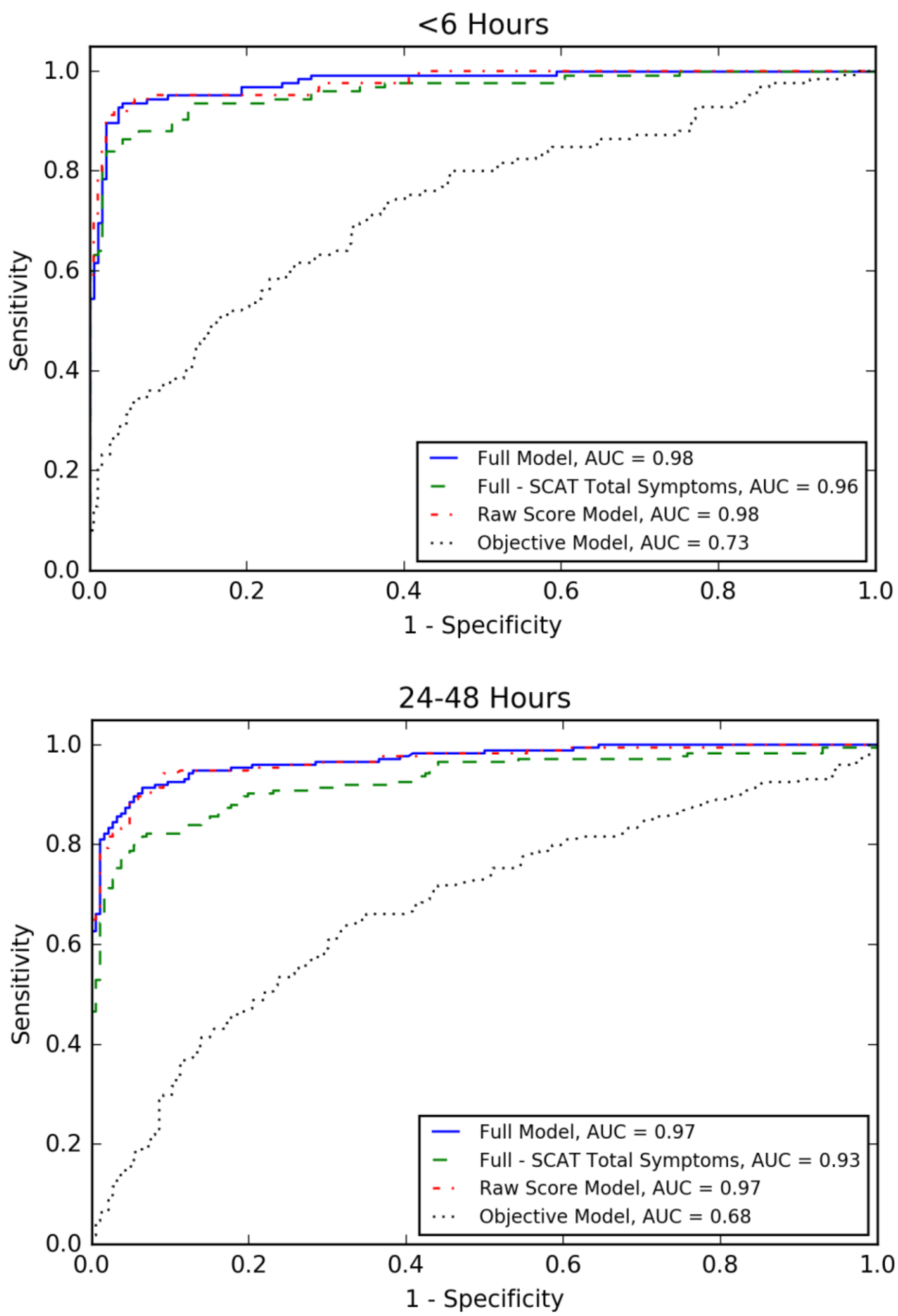

Figure 1: ROC curves for selected multivariate models based on validation against testing sets at <6 hours and 24-48 hours

The objective models for <6 hours and 24-48 hours contained the SAC and BESS assessments along with age. Using objective models instead of full models can result in losses up to 0.34 in sensitivity, 0.28 in specificity, and 0.29 in AUC. This loss in AUC is significant (p-value<0.001).

Finally, all models were validated against baseline data. The best univariate models achieved specificities ranging from 0.67-0.71 across <6 hours and 24-48 hours timepoints. Multivariate models did not demonstrate improved performance.

4 DISCUSSION

While logistic regression has been applied to other aspects of concussion management [45–47], this analysis is among the first applications to acute concussion assessment. This methodology combines individual risk modifiers and standard assessments to detect the acute effects of concussion – providing a single measure to guide injury assessment. The variables in both full models can be obtained within the time constraints of athletics, suggesting their potential application in sideline concussion management. These models were trained and validated on a larger sample of concussed athletes (n=560 for <6 hours and n=733 for 24-48 hours) compared to similar studies (n=40 to 166) [14,17,23,48–50].

The full models identify the effects of concussion more accurately than univariate models. This result supports previous studies, demonstrating that testing batteries provide more utility in acute concussion evaluation than any single assessment [14,17,23,48,49]. Both full models contained SAC, SCAT symptom assessments, and BESS. However, removing BESS from these models does not reduce AUC (p-value<0.001), suggesting that it provides little additional value beyond the SAC and SCAT symptom assessments. Conversely, removing SCAT total symptoms raw scores from each full model results in the greatest reduction in model performance, suggesting that symptoms better indicate acute concussion than neurological status and balance assessments. These results support previous studies which found that symptom assessments have higher sensitivity and specificity compared to neurocognitive and postural stability assessments [17,48–50].

These findings differ from Broglio et al., who found that neurocognitive assessments had higher sensitivity than symptom assessments [14]. These differences may be attributed to methodology and sample size. Broglio et al. used significant change from baseline (1 SD) to indicate concussion whereas this study used the logistic regression's estimates. The choice of 1 SD may create classification thresholds having higher sensitivity but also higher false-positive rates. Conversely, logistic regression models are optimized to minimize prediction error, leading to more balanced classification thresholds. Furthermore, a neurological status examination (i.e., SAC) was used in this study whereas Broglio et al. used computer-based neurocognitive examinations (i.e., Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), HeadMinder Concussion Resolution Index), and a pencil-and-paper neurocognitive battery. This study also used a 22-item SCAT symptom assessment compared to the 9-item symptom assessment used by Broglio et al., potentially explaining differences in sensitivity for symptom assessments. Finally, sensitivity estimates in this study are based on a much larger sample compared to Broglio et al. (n=75).

Unfortunately, relying on self-reported symptoms raises concern for symptom under-reporting, which may occur at rates up to 50% [43]. To account for this possibility in clinical settings, objective models were created by removing self-reported symptoms. Ultimately, these models were outperformed by all other multivariate models and the univariate models for SCAT symptom assessments, emphasizing the need for objective clinical measures which can better assess acute concussion. However, these findings may apply only to acute concussions; other studies found that symptom presentation and severity decline days after the injury while impairments in cognitive function and postural stability remain [17,41]. Differences in concussion presentation by timepoint motivated the separate analyses at <6 hours and 24-48 hours. Nonetheless, both full models were nearly identical so the time difference between <6 hours and 24-48 hours may be insufficient for detecting changes in concussion presentation.

Change scores for SAC and SCAT symptom severity appeared in both full models, suggesting their importance in a battery. Yet, BESS may be removed from full models with no significant loss in AUC. Full models have significantly greater AUC than raw score models, though this difference may not be practically significant. Univariate analysis showed similar performance between raw score and change score for the SAC and BESS. However, SCAT symptom assessment raw scores outperformed their change score counterparts. These results provide some quantitative support for the notion that neuropsychological assessments can be performed without baseline information [19], as expressed in the most recent consensus statement on concussion in sport [1]. Overall, these results mirror findings in similar studies. For instance, previous research has shown that incorporating baseline information leads to improved diagnostic accuracy on the SCAT battery, but these batteries can still perform at clinically acceptable levels when baseline information is unavailable [23,50]. Similar results were also found for other concussion assessment batteries, where raw scores and change scores typically agreed for acute concussion assessment [20,21]. Clinically speaking, these results imply that acute concussion assessment can still be performed accurately if baseline information is unavailable. This point is echoed in the most recent consensus statement [1], which states that "*baseline testing may be useful, but is not necessary for interpreting post-injury scores*." While our results provide evidence to support this statement at <6 hours and 24-48 hours, future studies should analyze the utility of baseline information in concussion assessment at timepoints beyond the acute stage, e.g., 1-2 weeks post-injury.

The analysis on age and number of previous concussions was largely inconclusive, as neither variable was significant in univariate analysis nor included in the full model. However, male sex was found to be significant in the full model (p-value < 0.05) and removing this variable from the full model results in reduced AUC (p-value < 0.001), suggesting the importance of considering sex differences in acute concussion assessment. The positive coefficient value associated with male sex suggests that, all else held equal, males have increased risk of acute concussion. Initially, this finding seems to contradict previous research which found female athletes to be at higher risk for concussion [25,51–53]. However, a post-hoc analysis of sex differences in the SAC, SCAT symptom assessments, and BESS at <6 hours and 24-48 hours

(Electronic Supplementary Material Appendix S3) shows that this result may instead suggest that males and females could achieve the same risk level even if a male athlete reports “better” performance on the assessments considered in the full model. For instance, the full model may consider a male athlete and female athlete to have the same acute concussion risk level even if the male reported fewer symptoms with less severity compared to the female. This interpretation supports previous findings which found female athletes to exhibit a greater symptom onset and cognitive decline compared to male athletes [24,26,50,53,54]. Clinically, these results suggest that males may still be concussed despite reporting lower symptom presentation and closer-to-normal neurocognitive deficits compared to females. This result also provides support for concussion assessment guidelines which are tailored by sex, as has been suggested by previous studies [24,54].

Multivariate models classified normal performances from baseline less accurately than those from unrestricted RTP. Symptom under-reporting during the RTP protocol may explain these results. Table 1 shows that mean SCAT symptom scores are higher at baseline than at unrestricted RTP (p-value<0.01). Since the models were trained on unrestricted RTP data, concussion probability was inflated for athletes reporting symptoms at baseline. Additionally, Table 1 shows that mean SAC and BESS scores were “worse” at baseline than at unrestricted RTP (p-value<0.01). Learning effects, i.e., improved performance from repetition, might explain these findings [13,55,56].

5 STUDY LIMITATIONS AND FUTURE WORK

By restricting training sets to the <6 hours, 24-48 hours, and unrestricted RTP timepoints, the models best distinguish between those groups. Additionally, study participants were NCAA athletes and Military Service Academy cadets, so future studies should investigate whether these models generalize to high school, recreational, or professional athletes. Furthermore, total scores were used for the SAC, SCAT symptom assessments, and BESS so future studies can investigate specific features of these assessments.

Finally, the selected risk modifiers and concussion assessments in this study are not exhaustive and, thus, future studies may consider other measures like the Sensory Organization Test, ImPACT, and CNS Vital Signs, in their analysis.

6 CONCLUSION

This study demonstrates the value of multidimensional assessment models such as the SCAT5, which incorporates the standard assessments considered in this study [18]. Logistic regression models were analyzed to determine which combinations of standard assessments best assess acute concussion. These models also provide a means to combine information from multiple concussion risk modifiers and standard assessments into a single measure which can be used to supplement clinical assessment decisions. Results suggest the importance of SCAT symptom assessments in acute concussion evaluation and support the use of assessment batteries over isolated assessments, though the BESS' value may be limited when SAC and SCAT symptom assessments are available. Additionally, change scores provide some clinical utility over raw scores, but acute concussion assessment can still be performed with sufficient accuracy when baseline information is unavailable. While further studies should generalize these models beyond NCAA athlete populations, this analysis can aid the future design of data-driven concussion assessment.

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8 COMPLIANCE WITH ETHICAL STANDARDS

8.1 Competing Interests

Gian-Gabriel Garcia, Steven Broglio, Mariel Lavieri, Thomas McAllister, and Michael McCrea declare that they have no conflict of interest.

8.2 Ethical Approval

This study was approved by each local Institutional Review Board and the Army Human Research Protection Office.

9 REFERENCES

1. McCrory P, Meeuwisse W, Dvorak J, Aubry M, Bailes J, Broglio S, et al. Consensus statement on concussion in sport—the 5 th international conference on concussion in sport held in Berlin, October 2016. Br. J. Sports Med. [Internet]. 2017;bjsports-2017-097699. Available from: http://bjsm.bmj.com/lookup/doi/10.1136/bjsports-2017-097699

2. Zuckerman SL, Kerr ZY, Yengo-Kahn A, Wasserman E, Covassin T, Solomon GS. Epidemiology of Sports-Related Concussion in NCAA Athletes From 2009-2010 to 2013-2014: Incidence, Recurrence, and Mechanisms. Am. J. Sports Med. [Internet]. 2015;43:2654–62. Available from: http://ajs.sagepub.com/cgi/content/short/43/11/2654

3. Giza CC, Kutcher JS, Ashwal S, Barth J, Getchius TSD, Gioia GA, et al. Summary of evidence-based guideline update: evaluation and management of concussion in sports: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology [Internet]. 2013;80:2250–7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3721093&tool=pmcentrez&rendertype=abstract

4. Broglio SP, Cantu RC, Gioia GA, Guskiewicz KM, Kutcher J, Palm M, et al. National Athletic Trainers' Association Position Statement: Management of Sport Concussion. J. Athl. Train. [Internet]. 2014;49:245–65. Available from: http://natajournals.org/doi/10.4085/1062-6050-49.1.07

5. Harmon KG, Drezner JA, Gammons M, Guskiewicz KM, Halstead M, Herring SA, et al. American Medical Society for Sports Medicine position statement: concussion in sport. Br. J. Sports Med. [Internet]. 2013;47:15–26. Available from: http://bjsm.bmj.com/cgi/doi/10.1136/bjsports-2012-091941

6. McCrory P, Meeuwisse WH, Kutcher JS, Jordan BD, Gardner A. What is the evidence for chronic

concussion-related changes in retired athletes: behavioural, pathological and clinical outcomes? Br. J. Sports Med. 2013;47:327–30.

7. Randolph C, Karantzoulis S, Guskiewicz K. Prevalence and characterization of mild cognitive impairment in retired national football league players. J. Int. Neuropsychol. Soc. [Internet]. 2013;19:873–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23902607

8. Guskiewicz KM, Marshall SW, Bailes J, McCrea M, Cantu RC, Randolph C, et al. Association between recurrent concussion and late-life cognitive impairment in retired professional football players. Neurosurgery [Internet]. 2005;57:719–26. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16239884

9. Daneshvar DH, Riley DO, Nowinski CJ, McKee AC, Stern RA, Cantu RC. Long-Term Consequences: Effects on Normal Development Profile After Concussion. Phys. Med. Rehabil. Clin. N. Am. 2011;22:683–700.

10. Kerr ZY, Marshall SW, Harding HP, Guskiewicz KM. Nine-Year Risk of Depression Diagnosis Increases With Increasing Self-Reported Concussions in Retired Professional Football Players. Am. J. Sports Med. 2012;40:2206–12.

11. Guskiewicz KM, Marshall SW, Bailes J, Mccrea M, Harding HP, Matthews A, et al. Recurrent concussion and risk of depression in retired professional football players. Med. Sci. Sports Exerc. 2007;39:903–9.

12. De Beaumont L, Lassonde M, Leclerc S, Théoret H. Long-term and cumulative effects of sports concussion on motor cortex inhibition. Neurosurgery. 2007;61:329–36.

13. Barr WB, McCrea M. Sensitivity and specificity of standardized neurocognitive testing immediately

following sports concussion. J. Int. Neuropsychol. Soc. 2001;7:693–702.

14. Broglio SP, Macciocchi SN, Ferrara MS. Sensitivity of the concussion assessment battery. Neurosurgery. 2007;60:1050–7.

15. Broglio SP, Ferrara MS, Sopiarz K, Kelly MS. Reliable change of the sensory organization test. Clin. J. Sport Med. [Internet]. 2008;18:148–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18332690

16. Lovell MR, Iverson GL, Collins MW, Podell K, Johnston KM, Pardini D, et al. Measurement of Symptoms Following Sports-Related Concussion: Reliability and Normative Data for the Post-Concussion Scale. Appl. Neuropsychol. [Internet]. 2006;13:166–74. Available from: http://www.tandfonline.com/doi/abs/10.1207/s15324826an1303_4

17. McCrea M, Barr WB, Guskiewicz K, Randolph C, Marshall SW, Cantu R, et al. Standard regression-based methods for measuring recovery after sport-related concussion. J. Int. Neuropsychol. Soc. 2005;11:58–69.

18. Echemendia RJ, Meeuwisse W, McCrory P, Davis GA, Putukian M, Leddy J, et al. The Sport Concussion Assessment Tool 5th Edition (SCAT5). Br. J. Sports Med. [Internet]. 2017;5:1–3. Available from: http://bjsm.bmj.com/lookup/doi/10.1136/bjsports-2017-097506

19. Randolph C. Baseline Neuropsychological Testing in Managing Sport-Related Concussion. Curr. Sports Med. Rep. [Internet]. 2011;10:21–6. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00149619-201101000-00009

20. Schmidt JD, Register-Mihalik JK, Mihalik JP, Kerr ZY, Guskiewicz KM. Identifying impairments after concussion: Normative data versus individualized baselines. Med. Sci. Sports Exerc. 2012;44:1621–8.

21. Echemendia RJ, Bruce JM, Bailey CM, Sanders JF, Arnett P, Vargas G. The utility of post-concussion neuropsychological data in identifying cognitive change following sports-related MTBI in the absence of baseline data. Clin. Neuropsychol. 2012;26:1077–91.

22. Valovich McLeod TC, Bay RC, Lam KC, Chhabra A. Representative baseline values on the Sport Concussion Assessment Tool 2 (SCAT2) in adolescent athletes vary by gender, grade, and concussion history. Am. J. Sports Med. 2012;40:927–33.

23. Putukian M, Echemendia R, Dettwiler-Danspeckgruber A, Duliba T, Bruce J, Furtado JL, et al. Prospective clinical assessment using sideline concussion assessment tool-2 testing in the evaluation of sport-related concussion in college athletes. Clin. J. Sport Med. 2015;25:36–42.

24. Covassin T, Elbin RJ, Harris W, Parker T, Kontos A. The Role of Age and Sex in Symptoms, Neurocognitive Performance, and Postural Stability in Athletes After Concussion. Am. J. Sports Med. [Internet]. 2012;40:1303–12. Available from: http://journals.sagepub.com/doi/10.1177/0363546512444554

25. Covassin T, Buz Swanik C, Sachs ML. Sex Differences and the Incidence of Concussions Among Collegiate Athletes. J. Athl. Train. [Internet]. 2003;38:238–44. Available from: www.journalofathletictraining.org

26. Covassin T, Schatz P, Swanik CB. Sex differences in neuropsychological function and post-concussion symptoms of concussed collegiate athletes. Neurosurgery. 2007;61:345–50.

27. Shehata N, Wiley JP, Richea S, Benson BW, Duits L, Meeuwisse WH. Sport concussion assessment tool: Baseline values for varsity collision sport athletes. Br. J. Sports Med. 2009;43:730–4.

28. Bruce JM, Echemendia RJ. Concussion history predicts self-reported symptoms before and following a concussive event. Neurology [Internet]. 2004;63:1516–8. Available from:

29. Covassin T, Stearne D, Elbin R. Concussion history and postconcussion neurocognitive performance and symptoms in collegiate athletes. J. Athl. Train. 2008;43:119–24.

30. Guskiewicz KM, Mccrea M, Marshall SW, Cantu RC, Randolph C, Barr W, et al. Cumulative Effects Associated With Recurrent Concussion in Football Players: The NCAA Concussion Study. J. Am. Med. Assoc. 2003;290:2549–55.

31. Broglio SP, McCrea M, McAllister T, Harezlak J, Katz B, Hack D, et al. A National Study on the Effects of Concussion in Collegiate Athletes and US Military Service Academy Members: The NCAA–DoD Concussion Assessment, Research and Education (CARE) Consortium Structure and Methods. Sport. Med. [Internet]. 2017;47:1437–51. Available from: http://link.springer.com/10.1007/s40279-017-0707-1

32. Carney N, Ghajar J, Jagoda A, Bedrick S, Davis-O'Reilly C, Du Coudray H, et al. Concussion guidelines step 1: Systematic review of prevalent indicators. Neurosurgery. 2014;75:3–15.

33. McCrory P, Meeuwisse WH, Aubry M, Cantu RC, Dvorák J, Echemendia RJ, et al. Consensus Statement on Concussion in Sport-The 4th International Conference on Concussion in Sport Held in Zurich, November 2012. Br. J. Sports Med. 2013;47:255–79.

34. Asken BM, McCrea MA, Clugston JR, Snyder AR, Houck ZM, Bauer RM. "Playing Through It": Delayed Reporting and Removal From Athletic Activity After Concussion Predicts Prolonged Recovery. J. Athl. Train. [Internet]. 2016;51:329–35. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27111584

35. Elbin RJ, Sufrinko AM, Schatz P, French J, Henry L, Burkhart S, et al. Removal From Play After Concussion and Recovery Time. Pediatrics [Internet]. 2016;138:e20160910–e20160910. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2016-0910

36. McCrea M, Kelly JP, Randolph C, Kluge J, Bartolic E, Finn G, et al. Standardized assessment of

concussion (SAC): on-site mental status evaluation of the athlete. J. Head Trauma Rehabil. 1998. p. 27–35.

37. Concussion in Sport Group. Sport Concussion Assessment Tool - 3rd Edition [Internet]. Br. J. Sports Med. 2013. p. 259. Available from: http://bjsm.bmj.com/cgi/content/long/47/5/259

38. Bell DR, Guskiewicz KM, Clark M a., Padua D a. Systematic Review of the Balance Error Scoring System. Sports Health [Internet]. 2011;3:287–95. Available from: http://journals.sagepub.com/doi/10.1177/1941738111403122

39. Van Buuren S, Boshuizen H, Knook D. Multiple imputation of missing blood pressure covariates in survival analysis. Stat. Med. [Internet]. 1999;18:681–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10204197%5Cnhttp://onlinelibrary.wiley.com/doi/10.1002/(SICI)1097-0258(19990330)18:6%3C681::AID-SIM71%3E3.0.CO;2-R/abstract

40. McCrea M, Guskiewicz KM, Marshall SW, Barr W, Randolph C, Cantu RC, et al. Acute effects and recovery time following concussions in collegiate football players. JAMA [Internet]. 2004;290:2556–63. Available from: http://bjsm.bmj.com/content/38/3/369.short

41. McCrea M, Guskiewicz K, Randolph C, Barr WB, Hammeke T a., Marshall SW, et al. Incidence, Clinical Course, and Predictors of Prolonged Recovery Time Following Sport-Related Concussion in High School and College Athletes. J. Int. Neuropsychol. Soc. [Internet]. 2013;19:22–33. Available from: http://www.journals.cambridge.org/abstract_S1355617712000872

42. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika. 1987;52:345–70.

43. Williamson IJS, Goodman D. Converging evidence for the under-reporting of concussions in youth ice hockey. Br. J. Sports Med. [Internet]. 2006;40:128–32. Available from:

http://bjsm.bmj.com/cgi/doi/10.1136/bjsm.2005.021832

44. Pepe MS, Longton G, Janes H. Estimation and comparison of receiver operating characteristic curves. Stata J. 2009;9:1–16.

45. Meehan WP, Mannix RC, Stracciolini A, Elbin RJ, Collins MW. Symptom Severity Predicts Prolonged Recovery after Sport-Related Concussion, but Age and Amnesia Do Not. J. Pediatr. [Internet]. 2013;163:721–5. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022347613002886

46. Sufrinko A, McAllister-Deitrick J, Womble M, Kontos A. Do Sideline Concussion Assessments Predict Subsequent Neurocognitive Impairment After Sport-Related Concussion? J. Athl. Train. [Internet]. 2017;52:1062–6050–52.4.01. Available from: http://natajournals.org/doi/10.4085/1062-6050-52.4.01

47. Sufrinko AM, Marchetti GF, Cohen PE, Elbin RJ, Re V, Kontos AP. Using Acute Performance on a Comprehensive Neurocognitive, Vestibular, and Ocular Motor Assessment Battery to Predict Recovery Duration After Sport-Related Concussions. Am. J. Sports Med. [Internet]. 2017;45:1187–94. Available from: http://journals.sagepub.com/doi/10.1177/0363546516685061

48. Register-Mihalik JK, Guskiewicz KM, Mihalik JP, Schmidt JD, Kerr ZY, McCrea M a. Reliable Change, Sensitivity, and Specificity of a Multidimensional Concussion Assessment Battery. J. Head Trauma Rehabil. [Internet]. 2013;28:274–83. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00001199-201307000-00005

49. Resch JE, Brown CN, Schmidt J, Macciocchi SN, Blueitt D, Cullum CM, et al. The sensitivity and specificity of clinical measures of sport concussion: three tests are better than one. BMJ Open Sport Exerc. Med. [Internet]. 2016;2:e000012. Available from: http://bmjopensem.bmj.com/lookup/doi/10.1136/bmjsem-2015-000012

50. Chin EY, Nelson LD, Barr WB, McCrory P, McCrea MA. Reliability and validity of the sport concussion assessment tool-3 (SCAT3) in high school and collegiate athletes. Am. J. Sports Med. 2016;44:2276–85.

51. Gessel LM, Fields SK, Collins CL, Dick RW, Comstock RD. Concussions among United States high school and collegiate athletes. J. Athl. Train. (National Athl. Trainers' Assoc. [Internet]. 2007;42:495–503. Available from: http://spot.lib.auburn.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=2009759920&site=ehost-live

52. Lincoln AE, Caswell S V., Almquist JL, Dunn RE, Norris JB, Hinton RY. Trends in Concussion Incidence in High School Sports. Am. J. Sports Med. [Internet]. 2011;39:958–63. Available from: http://journals.sagepub.com/doi/10.1177/0363546510392326

53. Dick RW. Is there a gender difference in concussion incidence and outcomes? Br. J. Sports Med. [Internet]. 2009;43:i46–50. Available from: http://bjsm.bmj.com/cgi/doi/10.1136/bjsm.2009.058172

54. Broshek DK, Kaushik T, Freeman JR, Erlanger D, Webbe F, Barth JT. Sex differences in outcome following sports-related concussion. J. Neurosurg. [Internet]. 2005;102:856–63. Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-20144363124&partnerID=40&md5=54d1cbc63fa313e46b3ee297ba55eb88

55. Valovich McLeod TC, Perrin DH, Guskiewicz KM, Shultz SJ, Diamond R, Gansneder BM. Serial administration of clinical concussion assessments and learning effects in healthy young athletes. Clin. J. Sport Med. 2004;14:287–95.

56. Moreau MS, Langdon J, Buckley T a. The lived experience of an in-season concussion amongst NCAA Division I student-athletes. Int. J. Exerc. Sci. [Internet]. 2014;7:62–74. Available from: http://digitalcommons.wku.edu/ijes/vol7/iss1/8