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Clinical study

Quantitative pupillometry in patients with traumatic brain injury and loss of consciousness: A prospective pilot study

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Objective: Loss of consciousness (LOC) is a hallmark feature in Traumatic Brain Injury (TBI), and a strong predictor of outcomes after TBI. The aim of this study was to describe associations between quantitative infrared pupillometry values and LOC, intracranial hypertension, and functional outcomes in patients with TBI.
Methods: We conducted a prospective study of patients evaluated at a Level 1 trauma center between November 2019 and February 2020. Pupillometry values including the Neurological Pupil Index (NPi), constriction velocity (CV), and dilation velocity (DV) were obtained.
Results: Thirty-six consecutive TBI patients were enrolled. The median (range) age was 48 (range 21–86) years. The mean Glasgow Coma Scale score on arrival was 11.8 (SD = 4.0). DV trichotomized as low (<0.5 mm/s), moderate (0.5–1.0 mm/s), or high (>1.0 mm/s) was significantly associated with LOC ($P = .02$), and the need for emergent intervention ($P < .01$). No significant association was observed between LOC and NPi ($P = .16$); nor between LOC and CV ($P = .07$).
Conclusions: Our data suggests that DV, as a discrete variable, is associated with LOC in TBI. Further investigation of the relationship between discrete pupillometric variables and NPi may be valuable to understand the clinical significance of the pupillary light reflex findings in acute TBI.

1. Introduction

Concussion is a form of traumatic brain injury (TBI) that is poorly understood and often difficult to diagnose due to heterogenous presenting symptoms. The Concussion Guidelines put forth in 2014 [1], from a systematic review of the literature, named disorientation, impaired balance, slower reaction time, and impaired verbal learning and memory as prevalent and consistent indicators of concussion. Although concussion is not defined by loss of consciousness (LOC) [2], brief periods of impaired consciousness are often a significant feature and are strongly predictive of patient outcome [3].

Assessment of the pupillary light reflex (PLR) is critical in the evaluation of TBI and provides important prognostic information in unresponsive patients [4]. Conventionally, the PLR exam is interpreted subjectively, with various descriptors denoting normal or abnormal responses (e.g., brisk, sluggish, fixed) [5]. The advent of handheld quantitative infrared pupillometer devices has provided a way for standardized PLR measurement in a manner that will

Abbreviations: TBI, traumatic brain injury; LOC, loss of consciousness; NPi, The Neurological Pupil Index; CT, computed tomography; IRB, institutional review board; ICP, intracranial pressure; EVD, external ventriculostomy; GCS, Glasgow coma scale; mRS, modified Rankin scale; DV, dilation velocity; MIN, minimum pupil diameter at peak constriction; % CH, percent of change; MCV, maximum constriction velocity; LAT, latency of constriction; CV, constriction velocity; PLR, pupillary light reflex.

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eliminate inter-examiner inconsistencies and improve measurement precision, particularly in the context of sedatives [6]. Specifically, the Neurological Pupil Index (NPi), calculated from pupil size and latency as well as constriction velocity (CV) and dilation velocity (DV) and has been studied in various environments [7–11].

There is emerging data suggesting that automated pupillometry measurement is not only reliable in the neurocritical care setting [12], but is an early predictor of outcomes in patients with TBI [13,14], stroke [15], anoxic encephalopathy after cardiac arrest [16], and aneurysmal subarachnoid hemorrhage [17]. A previous study by our group described the value of pupillometry as a triage tool for blunt severe TBI [14]. Herein, we evaluate the association of the NPi, as well as discrete pupillometric values, with loss of consciousness and subsequent outcomes following TBI. We hypothesized that loss of consciousness in the setting of TBI would be associated with automatic pupillometry measurements in a detectable and significant fashion.

2. Methods

2.1. Study Design, Setting, & participants

This study was performed under an Institutional Review Board (IRB) approved protocol in compliance with institutional regulations with regard to the study of human subjects (IRB number STU072017-046). Because PLR assessment is standard-of-care, a waiver of consent was granted. This prospective study enrolled consecutive TBI patients that required neurosurgical evaluation for TBI between November 2019 and February 2020 at a Level 1 trauma center. All patients with blunt TBI and any abnormality on computed tomography (CT) of the head were enrolled. We limited patient inclusion to those who had a CT scan with an abnormality because these individuals would fall under the umbrella of Neurosurgery and would generate a Neurosurgery consult, that would enable us to obtain pupillometry measurements upon arrival. Initial pupillometry readings were obtained for each eye by the on-call neurosurgery resident during the first neurological examination in the emergency department (ED) trauma hall. Patients with penetrating brain injuries were excluded; as were patients with severe orbit or eye injuries. A NeurOptics NPi-200 (NeurOptics, Inc.) device was used for all pupillometry readings.

The following variables were obtained prospectively from enrolled patients: age, sex, trauma velocity, presence of LOC prior to- or at the time of- ED admission, pattern of injury, need for an emergent procedure such as the placement of an intracranial pressure (ICP) monitor or an external ventricular drain (EVD), or a surgical decompression, presence of increased intracranial pressure (ICP), Glasgow coma scale (GCS) score on arrival, and toxicology screen results.[32] LOC was self-reported by the patient or by the paramedic team transporting the patient from scene to ED. We also reported whether the patient was intubated at the time of initial pupillometry assessment as well as agents used for rapid sequence intubation. With respect to trauma velocity, motor vehicle collisions and falls from height were defined as high impact velocity injuries. Low impact velocity injuries consisted of assaults and falls from standing. Modified Rankin scale (mRS) score was recorded for all patients three months after injury [18].

Pupillometry parameters obtained included the following: NPi; pupil size prior to light stimulus; anisocoria (>1 mm); latency of constriction (LAT; or time of onset of constriction following initiation of the light stimulus, measured in fractions of a second); both average CV and maximum constriction velocity (MCV) of constriction of the pupil diameter responding to the flash of light (measured in mm/sec); DV (average velocity of the pupil during the dilation phase when, after having reached the peak of constriction, the pupil dilates back to the initial resting size, measured in mm/sec); minimum pupil diameter at peak constriction (MIN), and percent of change (size – MIN / size as a percent; %CH);. The PLR was scored as normal if the NPi was ≥ 3.0 and abnormal if the NPi was < 3.0 [5]. Similarly, CV categorized as normal (≥0.8 mm/s) or abnormal (<0.8 mm/s) [19]. DV was trichotomized as low (<0.5 mm/s), moderate (0.5–1.0 mm/s), or high values (>1.0 mm/s). Table 1 and Fig. 1 summarize the pupillary measurement parameters evaluated as described by previous research [20]. Parameters were reported for each eye. Good functional outcome was defined as mRS ≤ 3 at 30 days post-injury [21].

2.2. Statistical analysis

Statistical analysis was completed in R using the *exact2x2* [22] and *DescTools* [23] packages. A Fisher exact test was used to evaluate the relationship of contingency tables with binomial variables. A Cochran-Armitage test was used to evaluate contingency tables with binomial and ordinal variables. A p value < 0.05 was considered significant for all analyses.

3. Results

3.1. Patient characteristics

Thirty-six consecutive patients were enrolled. The median age of the cohort at presentation was 48 years (range 21–86 years). High-impact velocity injuries were observed in 50% (n = 18) of the cohort. Nine patients underwent emergency procedures including: EVD placement (1), ICP monitor placement (4), and emergent decompressive craniotomy with or without craniectomy for hematoma evacuation (4). One patient underwent a craniotomy the day following ED presentation. The mRS at 3 months post injury was 0 for the majority of the cohort (n = 28), and there were 3 deaths (mRS = 6) observed. Additional demographic information for this cohort has been published elsewhere [14].

3.2. Outcomes

DV was significantly associated with LOC (Cochran-Armitage test for trend, P = .02) (Table 2). No significant relationship was identified between NPi and LOC (Fisher exact test, p = .16). No significant relationship was identified between CV and LOC (Fisher

Table 1
NeurOptics NPi-200 pupillary measurement parameters.

Parameter	Description	Comments
Size	Maximum Diameter	Maximum pupil size before constriction
MIN	Minimum Diameter	Pupil diameter at peak constriction
% CH = % Change	% of change (Size-MIN) / Size as a %	
LAT = Latency of Constriction	Time of onset of constriction following initiation of the light stimulus	Measured in fractions of a second
CV = constriction velocity	Average speed of pupillary diameter reduction	Measured in millimeters per second
MCV = Maximum Constriction Velocity	Maximum velocity of pupil constriction of the pupil diameter responding to the flash of light	Measured in millimeters per second
DV = Dilation Velocity	The average pupillary velocity when, after having reached the peak of constriction, the pupil tends to recover and dilate back to the initial resting size	Measured in millimeters per second

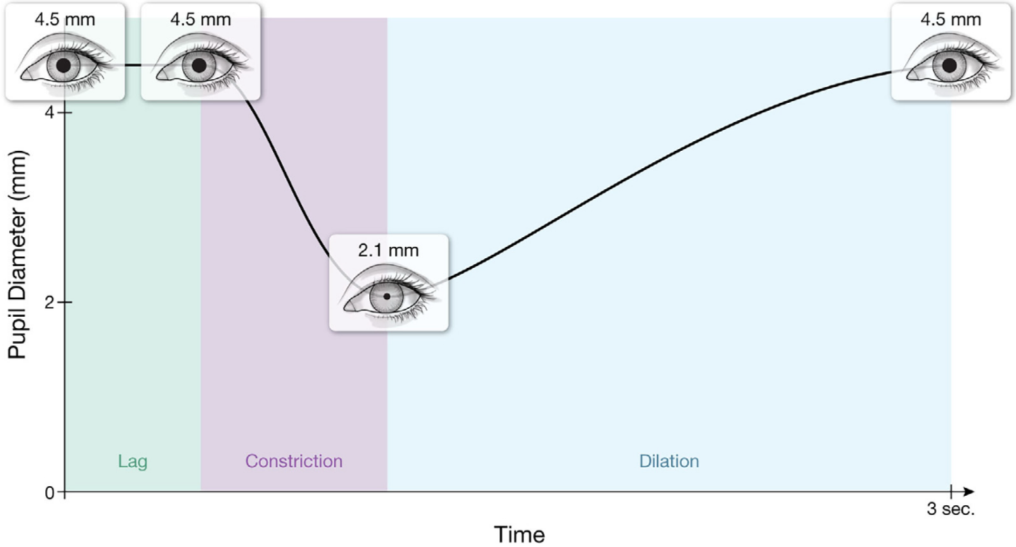

Fig. 1. Graph showcasing the different phases of pupillary reactivity after light stimulation.

Table 2
Contingency table: Dilation velocity and Loss of Consciousness (LOC).

DV – LOC				
LOC	Low DV	Moderate DV	High DV	Total
Yes	12	8	4	24
No	0	5	3	8
Total	12	13	7	32
p = .02				
DV available for n = 32 patients				

exact test, *P* = .07). A significant relationship was identified between NPi and increased ICP (Fisher exact test, *P* < .01). There was no association appreciated between DV and increased ICP evidenced by EVD, ICP monitor, or decompressive surgery (Cochran-Armitage test for trend, *P* = .34). CV was not associated with increased ICP (Fisher exact test, *P* = .17). DV was significantly associated with subsequent emergency procedures (EVD/ICP monitor placement or surgery) (Cochran-Armitage test for trend, *P* < .01). Similarly, both NPi and CV were also significantly associated with the need for an emergency procedure (Fisher exact test, *P* < .01). A normal NPi was associated with good functional outcome ($mRS \leq 3$) at 90 days (Fisher exact test, *P* = .02) (Table 3). No association was identified between DV and functional outcome at 90 days (Cochran-Armitage test for trend, *P* = .09). Conversely, a faster CV was significantly associated with a better 3-month functional outcome (Fisher exact test, *P* = .03).

4. Discussion

An accurate assessment of the PLR remains essential to the evaluation of the TBI patient [24,25]. This assessment is a non-invasive and objective way to obtain information on the neuronal dynamics of both cerebral hemispheres [19]. Several studies have established pupillary reactivity to be one of the strongest predictors of outcome after TBI [26–28]. Although early studies reported acceptable inter-observer agreement in the assessment of pupillary reactivity by clincal examiner [29], more robust publications have reported inadequate interrater reliability and limited validity for subjective scoring of pupillary assessments [30,31]. Thus, automated pupillometry holds value in standardizing pupil examinations between different providers and enables the detection of subtle changes in pupillary responsiveness. Moreover, earlier detection of abnormal pupillary reactions with quantitative pupillometry can facilitate earlier intervention and a better prognosis [32].

In the setting of TBI, abnormal pupillary reactivity via traditional light examination is used as a surrogate for elevated ICP and thereby influences clinical decision-making [33,34]. NPi is therefore increasingly being explored as a prognostic tool in TBI and found to be highly correlated with ICP [35,36]. Specifically, a significant association between NPi and refractory ICP measured via invasive monitoring requiring decompressive craniectomy and poor six-month outcomes have been reported [13]. Conversely, other studies have reported a weak, statistically insignificant relationship between NPi and invasive ICP measures [37]. A recent pilot study has described a significant association of NPi with subsequent emergent intervention (EVD/ICP monitor placement or decompressive surgery) and 90 day functional outcome when incorporated into triage and assessment of TBI patients [14].

Our study is the first to investigate the association of NPi, CV, and DV with LOC, specifically, as well as ICP, intervention, and three-month functional outcome in the setting of blunt TBI. Concussion is traditionally difficult to diagnose and has heterogenous presenting symptoms and sequelae [1]. Although concussion is not defined by LOC [2], brief periods of impaired or absent consciousness are often a significant feature. Mild and moderate TBI, which include the diagnosis of concussion, both have LOC in their diagnostic criteria [38,39]. The duration of LOC corresponds to TBI severity and is strongly predictive of patient outcome [3]. Several studies have reported decreased CV and DV in patients with mild TBI [40–42]. Although the NPi algorithm incorporates several pupillary reaction variables, we did not observe a significant relationship between NPi and loss of consciousness in patients with a GCS >13 after TBI. DV, on the other hand, was significantly

Table 3
Contingency table: Neurological Pupil Index (NPi) and functional outcome.

NPi – functional outcome			
Functional Outcome	Abnormal NPi	Normal NPi	Total
Good ($mRS \leq 3$)	3	28	31
Poor ($mRS > 3$)	3	2	5
Total	6	30	6
p = .02			

associated with LOC after TBI. Interestingly, a 2019 study [43] of pupillary changes in asymptomatic high school football athletes reported a significant relationship with DV but not NPi following high-acceleration head impacts. DV has also been shown to have a direct relationship with GCS following TBI and may represent a discrete injury biomarker [44].

The NPi represents a summary score of pupillometric values for several variables and alone is insufficient to explain complete or subtle variance normal following TBI. For example, a significant mismatch between NPi and CV values has been reported in as high as 17% of readings even with pupillometry, indicating that the relative speed at which the pupil changes size (e.g., brisk or sluggish), even when measured with quantitative pupillometric devices (CV in mm/s) is insufficient to rule in or out an abnormal PLR [19]. Normal values for NPI and CV were associated in our cohort to good functional outcome at 3 months.

An understanding of the role of the discrete elements of the PLR will be valuable moving forward in the prognostication of patients with TBI. This study showcases the potential applications of quantitative pupillometry in the setting of head trauma. Further understanding of the individual components of the PLR will allow us to characterize different patterns of brain injury better, spanning from severe brain trauma requiring a surgical intervention, to milder insults. The future study of pupillometry should include milder injury that does not necessarily result in frank LOC, and reflect common concussions seen on the sports field or even the battlefield. Ideally, quantitative pupillometry would allow us to follow patients with brain injury over time to monitor recovery, and to reduce the morbidity resulting from post-concussive disorders.

4.1. Limitations

This study is primarily limited by a small sample size (n = 36). Additionally, the mechanism of injury and presence of substances were not controlled for and may have affected pupillometric values. Also, LOC was determined by patients who remember losing consciousness, or by first response teams on the field who saw the patient unconscious, and some instances of LOC may have been missed. Finally, some pupillometric values have been reported to change with age [45], thus future studies may require correction for demographic variables. We also had few mild injuries, and our results may not apply to common concussions that do are not associated with LOC. Despite these limitations, our study is benefited by a prospective and consecutive nature of data collection and is the first study of its kind to report on the associations of NPi, CV, and DV with LOC, ICP, and functional outcome in the setting of blunt TBI.

5. Conclusion

Quantitative pupillometry is increasingly utilized in the assessment of patients with TBI. Our data suggests that DV as a discrete variable was associated with LOC in TBI patients and may represent a potential injury biomarker in addition to NPi. Further investigation of the relationship between discrete pupillometric variables may be valuable to understanding the elements of the PLR.

6. Disclosure of funding

This study was funded by the University of Texas Southwestern department of Neurosurgery, and the University of Texas Southwestern department of Nursing.

7. IRB compliance statement and ethical adherence

This study was written in compliance with our institutional ethical review board (IRB #STU-072017-046).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] 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. Lippincott Williams and Wilkins; 2014.
[2] Ommaya AK, Gennarelli TA. Cerebral concussion and traumatic unconsciousness. Brain 1974;97:633–54.
[3] Forde CT, Karri SK, Young AMH, Ogilvy CS. Predictive markers in traumatic brain injury: opportunities for a serum biosignature. Br J Neurosurg 2014:8–15.
[4] Ortega-Perez S, Shoyombo I, Aiyagari V, Atem F, Hill M, Stutzman SE, et al. Pupillary light reflex variability as a predictor of clinical outcomes in subarachnoid hemorrhage. J Neurosci Nurs 2019;51:171–5.
[5] Olson DWM, Fishel M. The use of automated pupillometry in critical care. W.B. Saunders 2016:101–7.
[6] Du R, Meeker M, Bacchetti P, Larson MD, Holland MC, Manley GT. Evaluation of the portable infrared pupillometer. Neurosurgery 2005;57:198–203.
[7] Zhao W, Stutzman S, DaiWai O, Saju C, Wilson M, Aiyagari V. Inter-device reliability of the NPi-100 pupillometer. J Clin Neurosci 2016;33:79–82.
[8] Olson DM, Stutzman SE, Atem F, Kincaide JD, Ho TT, Carlisle BA, et al. Establishing normative data for pupillometer assessment in neuroscience intensive care: the "eND-PANIC" registry. J Neurosci Nurs 2017;49:251–4.
[9] Mazhar K, Olson DM, Atem FD, Stutzman SE, Moreno J, Venkatachalam A, et al. Supratentorial intracerebral hemorrhage volume and other CT variables predict the neurological pupil index. Clin Neurol Neurosurg 2021;200:106410.
[10] Weerakoon SM, Stutzman SE, Atem FD, Kuchenbecker KS, Olson DM, Aiyagari V. Investigation of pupillary changes after carotid endarterectomy and carotid stent placement using automated pupillometry. J Stroke Cerebrovasc Dis 2020;29:104693.
[11] Obinata H, Yokobori S, Shibata Y, Takiguchi T, Nakae R, Igarashi Y, et al. Early automated infrared pupillometry is superior to auditory brainstem response in predicting neurological outcome after cardiac arrest. Resuscitation 2020;154:77–84.
[12] Couret D, Boumaza D, Grisotto C, Triglia T, Pellegrini L, Ocquidant P, et al. Reliability of standard pupillometry practice in neurocritical care: an observational, double-blinded study. Crit Care 2016;20:99.
[13] Jahns FP, Miroz JP, Messerer M, Daniel RT, Taccone FS, Eckert P, et al. Quantitative pupillometry for the monitoring of intracranial hypertension in patients with severe traumatic brain injury. Crit Care 2019;23.
[14] El Ahmadieh TY, Bedros N, Stutzman SE, Nyancho D, Venkatachalam AM, MacAllister M, et al. Automated pupillometry as a triage and assessment tool in patients with traumatic brain injury. World Neurosurgery. 2020;145.
[15] Kim TJ, Park SH, Jeong HB, Ha EJ, Cho WS, Kang HS, et al. Neurological pupil index as an indicator of neurological worsening in large hemispheric strokes. Neurocrit Care 2020;33:575–81.
[16] Oddo M, Sandroni C, Citerio G, Miroz J-P, Horn J, Rundgren M, et al. Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double-blinded study. Intensive Care Med 2018;44:2102–11.
[17] Aoun SG, Stutzman SE, Vo PUN, El Ahmadieh TY, Osman M, Neeley O, et al. Detection of delayed cerebral ischemia using objective pupillometry in patients with aneurysmal subarachnoid hemorrhage. J Neurosurg 2020;132:27–32.

[18] Van Swieten JC, Koudstaal PJ, Visser MC, Schouten H, Van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604–7.
[19] Shoyombo I, Aiyagari V, Stutzman SE, Atem F, Hill M, Figueroa SA, et al. Understanding the relationship between the neurologic pupil index and constriction velocity values. Sci Rep 2018;8.
[20] Lussier BL, Stutzman SE, Atem F, Venkatachalam AM, Perera AC, Barnes A, et al. Distributions and reference ranges for automated pupillometer values in neurocritical care patients. J Neurosci Nurs 2019;51:335–40.
[21] Hanley DF, Lane K, McBee N, Ziai W, Tuhrim S, Lees KR, et al. Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial. Lancet 2017;389:603–11.
[22] Fay MP. Confidence intervals that match fisher's exact or blaker's exact tests. Biostatistics 2010;11:373–4.
[23] Signorell A. Tools for Descriptive Statistics [R package DescTools version 0.99.39]. 2020.
[24] Braakman R, Gelpke GJ, Habbema JDF, Maas AIR, Minderhoud JM. Systematic selection of prognostic features in patients with severe head injury. Neurosurgery 1980;6:362–70.
[25] Brennan PM, Murray GD, Teasdale GM. Simplifying the use of prognostic information in traumatic brain injury. Part 1: The GCS-Pupils score: an extended index of clinical severity. J Neurosurg 2018;128:1612–20.
[26] Han J, King NKK, Neilson SJ, Gandhi MP, Ng I. External validation of the CRASH and IMPACT prognostic models in severe traumatic brain injury. J Neurotrauma 2014;31:1146–52.
[27] Khanna R, Harris DA, McDevitt JL, Fessler RG, Carabini LM, Lam SK, et al. Impact of anemia and transfusion on readmission and length of stay after spinal surgery: a single-center study of 1187 operations. Clin Spine Surg 2017;30:E1338–42.
[28] Steyerberg EW, Mushkudiani N, Perel P, Butcher I, Lu J, McHugh GS, et al. Predicting outcome after traumatic brain injury: Development and international validation of prognostic scores based on admission characteristics. PLoS Med 2008;5:1251–61.
[29] Van Den Berge JH, Schouten HJA, Boomstra S, Van Drunen LS, Braakman R. Interobserver agreement in assessment of ocular signs in coma. J Neurol Neurosurg Psychiatry 1979;42:1163–8.
[30] Clark A, Clarke TNS, Gregson B, Hooker PNA, Chambers IR. Variability in pupil size estimation. Emerg Med J 2006;23:440–1.
[31] Olson DWM, Stutzman S, Saju C, Wilson M, Zhao W, Aiyagari V. Interrater reliability of pupillary assessments. Neurocrit Care 2016;24:251–7.
[32] Mader MM, Piffko A, Dengler NF, Ricklefs FL, Dührsen L, Schmidt NO, et al. Initial pupil status is a strong predictor for in-hospital mortality after aneurysmal subarachnoid hemorrhage. Sci Rep 2020;10:1–11.
[33] Alali AS, Temkin N, Barber J, Pridgeon J, Chaddock K, Dikmen S, et al. A clinical decision rule to predict intracranial hypertension in severe traumatic brain injury. J Neurosurg 2019;131:612–9.
[34] Chesnut RM, Temkin N, Dikmen S, Rondina C, Videtta W, Petroni G, et al. A Method of managing severe traumatic brain injury in the absence of intracranial pressure monitoring: the imaging and clinical examination protocol. J Neurotrauma 2018;35:54–63.
[35] McNett M, Moran C, Grimm D, Gianakis A. Pupillometry trends in the setting of increased intracranial pressure. J Neurosci Nurs 2018;50:357–61.
[36] Al-Obaidi SZ, Atem FD, Stutzman SE, Olson DM. Impact of increased intracranial pressure on pupillometry: a replication study. Crit Care Explor. 2019;1:e0054-e.
[37] Stevens AR, Su Z, Toman E, Belli A, Davies D. Optical pupillometry in traumatic brain injury: neurological pupil index and its relationship with intracranial pressure through significant event analysis. Brain Inj 2019;33:1032–8.
[38] VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury. J Rehabil Res Dev 2009;46:Cp1-68.
[39] Hoffman H, Furst T, Jalal MS, Chin LS. Costs and predictors of 30-day readmissions after craniotomy for traumatic brain injury: a nationwide analysis. J Neurosurg 2019;1–9.
[40] Capó-Aponte JE, Urosevich TG, Walsh DV, Temme LA, Tarbett AK. Pupillary Light Reflex as an Objective Biomarker for Early Identification of Blast-Induced mTBI. J Spine 2013:4.
[41] Ciuffreda KJ, Joshi NR, Truong JQ. Understanding the effects of mild traumatic brain injury on the pupillary light reflex. Concussion. 2017;2:CNC36-CNC.
[42] Thiagarajan P, Ciuffreda KJ. Pupillary responses to light in chronic non-blast-induced mTBI. Brain Inj 2015;29:1420–5.
[43] Joseph JR, Swallow JS, Willsey K, Almeida AA, Lorincz MT, Fraumann RK, et al. Pupillary changes after clinically asymptomatic high-acceleration head impacts in high school football athletes. J Neurosurg 2020;133:1886–91.
[44] Thakur B, Nadim H, Atem F, Stutzman SE, Olson DWM. Dilation velocity is associated with Glasgow Coma Scale scores in patients with brain injury. Brain Inj 2020.
[45] Tekin K, Sekeroglu MA, Kiziltoprak H, Doguizi S, Inanc M, Yilmazbas P. Static and dynamic pupillometry data of healthy individuals. Clin Experiment Optometry 2018;101:659–65.