Evaluating the Reliability of Neurological Pupillary Index as a Prognostic Measurement of Neurological Function in Critical Care Patients

California University of Science and Medicine
School of Medicine

Muhammad Ghauri[1], Arisa Ueno[1], Sumayya Mohammed[1], Daniel Miulli[2], Javed Siddiqi[1,2]

[1]School of Medicine, California University of Science and Medicine, Colton, CA

[2]Department of Neurosurgery, Arrowhead Regional Medical Center, Colton, CA

ARROWHEAD REGIONAL MEDICAL CENTER

ABSTRACT

Background: Neurological pupil index (NPi) is a novel method of assessing pupillary size and reactivity using pupillometry to reduce human subjectivity. This paper aims to establish NPi as a good prognostic factor in neurological diseases by observing the correlation between NPi, modified Rankin Scale (mRS), and Glasgow Coma Scale (GCS)

Methods: The data was collected in the neuro ICU at Arrowhead Regional Medical Center on 194 patients to fulfill our pre-study power calculation. We utilized the Kolmogorov-Smirnova and Shapiro-Wilk normality tests with Lilliefors significance correction. Pearson product-moment correlation was performed between average final NPi and final GCS. Multi-variate linear regression and analysis of variance (ANOVA) were used to evaluate the association and predictive capabilities of NPi on GCS and discharge mRS. Finally, we evaluated whether age, ethnicity, sex, length of stay (LOS), or discharge location were significantly associated with NPi.

Results: We observed a significant correlation between final GCS, NPi (r=.609, p<0.001), and discharge mRS (r=-0.724, p<0.001). Discharge mRS had a significant correlation with discharge location (r=0.454, p<0.001), average final NPi (r=-0.495, p<0.001), and final GCS (r=-0.724, p<0.001). Our regression analysis revealed that NPi significantly predicted GCS and mRS scores; however, no associations were found between age, ethnicity, sex, LOS, or discharge location. Limitations of our study include a single institutional study with a lack of disease subtyping and the inability to quantify the predictive ability of NPi.

Conclusions: This study examined the correlation between NPi and the prognosis of neuro ICU patients at ARMC in San Bernardino County, CA. Our results demonstrated a significant predictive association between average final NPi, final GCS, and discharge mRS scores. The relationship between these variables suggests that NPi measurements could be used similarly to GCS as an effective predictor of prognosis. Our results indicate that NPi is a promising tool in our armamentarium to gauge a patient's neurological health, monitor disease/treatment progression, and better predict prognosis in modern neurocritical practice.

INTRODUCTION

Pupillary size and reactivity are the major noninvasive methods of assessing neurological function. During the pupillary light reflex exam, we measure the optic and oculomotor nerve reflex to assess the brainstem function (Figure 1). The pupil's size and symmetry are measured, and the rate of reactivity is classified as either brisk, sluggish, or non-reactive. Abnormal measurements can indicate pathologies such as stroke, tumors, and brain injuries (1,2,6).

Current methods of assessing pupillary reflex include the Glasgow Coma Scale (GCS) and modified Rankin Scale (mRS). To date, many variations of these clinical tools have been developed to further refine the prognosticative ability of patient outcomes. However, these measurements are predisposed to inaccuracy due to subjectivity, inexperience, language barriers, iatrogenic barriers (e.g., intubation, sedation), and lack of standardization of the examiner [5-9]. Neurological pupil index (NPi) is a new practice established by NeuroOptics, Inc. (Irvine, USA) that measures the size, latency, and velocity parameters and quantifies them on a scale from zero to five, zero being non-reactive, and a score equal to or above three indicating normal pupil behavior [6]. NPi utilizes automated pupillometry to decrease human subjectivity and minimize administration time to increase the efficiency and accuracy of neurological assessments. Evaluating the change in NPi could potentially serve as a more robust prognostication tool to assess the recovery of the brain in neurocritical care.

If we can establish a correlation between NPi, mRS, and GCS, it could support the reliability of NPi as an alternative and potentially more robust prognostic tool in critical care patients. In this study, we used a pupillometer to measure the NPi in 194 subjects in the neurosurgical intensive care unit (ICU) at Arrowhead Regional Medical Center (ARMC) in San Bernardino, California. We hypothesized that NPi and GCS would be positively correlated, mRS and NPi would be negatively correlated, and NPi could significantly predict GCS and mRS scores. Therefore, NPi can be used similarly to or in conjunction with GCS as a tool to assess neurologic function across a varied neurocritical patient population.

METHODS

Data Collection

We collected data from patients in the neuro ICU at Arrowhead Regional Medical Center. The following demographic and clinical information were obtained from medical records to describe patient baseline characteristics: age, sex, ethnicity, length of stay (LOS), and discharge location. Clinical neurological assessments were obtained using conventional established methods upon admission and at the time of discharge. NPi measurements were obtained every four hours (and every hour for unstable patients) using the NeuroOptics Pupillometer.

Statistical Analyses

Initially, we conducted a pre-study power calculation to compute the statistically significant sample size needed for data collection. Next, we evaluated the homogeneity of our data distribution by using the Kolmogorov-Smirnova and Shapiro-Wilk normality tests with Lilliefors significance correction. We then performed Pearson product-moment correlation analyses to identify any statistically significant correlations between our continuous variables average final NPi, Final GCS, and LOS. The obtained Pearson correlation coefficients were categorized as weak (0.00-0.30), moderate (0.31-0.60), and strong (>0.60). The association of NPi, GCS, and mRS and the ability of NPi to predict GCS and mRS, was determined using multiple and ordinal regression analysis. Finally, we determined whether several predictor variables, such as age, ethnicity, sex, LOS, and discharge location, could significantly predict a patient's NPi score using multivariate regression and ANOVA. All statistical analyses were performed using SPSS statistics software V28.0.1.0 (IBM Inc., Armonk, USA).

RESULTS

Table 1. Patient Demographics/Characteristics

Variable	Value (n=193)
Age	62.44 ± 14
Sex	
Male	111 (57.5%)
Female	82 (42.5%)
Ethnicity	
Asian	11 (5.7%)
African American	30 (15.5%)
Caucasian	30 (15.5%)
Hispanic	117 (60.6%)
Pacific Islander	1 (0.5%)
Other	2 (0.5%)
Unknown	2 (1%)
Initial GCS	14.28 ± 1.61
Final GCS	14.38 ± 1.59
Delta GCS	0.098 ± 0.98
Initial NPi	
Left	4.36 ± 0.61
Right	4.37 ± 0.51
Avg	4.36 ± 0.22
Final NPi	
Left	4.36 ± 0.66
Right	4.34 ± 0.59
Avg	4.35 ± 0.32
Delta NPi	
Left	-0.0004
Right	-0.0233
Avg	-0.0118 ± 0.28
Initial mRS	2.36 ± 1.62
Final mRS	2.35 ±1.72
Delta mRS	0.0052 ± 1.03
Length of Stay (LOS)	7.25 ± 9.21
Discharge Location	
AMA	5 (2.59%)
EXPIRED	3 (1.55%)
HOME	121 (62.69%)
HOSPICE	2 (1.04%)
INPT TO OSH	7 (3.63%)
LTAC	1 (0.52%)
REHAB	27 (14%)
SNF	20 (10.36%)

Patient demographics/characteristics were obtained at baseline (Table 1). Categorical variables (age, sex, ethnicity, sex, discharge location) were reported as frequencies and percentages. Continuous variables (initial/final/average GCS, NPi, mRS, LOS) were described as mean and standard deviation.

Our statistical analysis revealed a homogeneous distribution of data by age, sex, ethnicity, final GCS, average final NPI, final mRS, LOS, and discharge location. Table 2 summarizes the correlation coefficients obtained from our statistical models. We identified a significant correlation between NPi, GCS (r=0.609, p<0.001), and mRS (r=-0.495, p<0.001). Regression analysis was also used to test if NPi could significantly predict GCS, and discharge mRS score. The overall regression analyses were statistically significant for GCS (R^2=0.37, F(331,561)=112.01, p≤0.001) and discharge mRS (R^2=0.241, F(213, 657) = 112.01, p≤0.001). Table 3 outlines the results of our multiple regression and ANOVA models used to identify associations between NPi and predictors of age, sex, ethnicity, LOS, and discharge location. Although our model was statistically significant, when looking at the unique individual contribution of our predictors, we found that age, ethnicity, sex, LOS, and discharge location (DL) displayed no significant associations or ability to predict NPi.

RESULTS

Strong Correlation
Moderate Correlation
Weak Correlation

	Avg Final Npi	Final GCS	Discharge mRS	LOS	Discharge Location	Sex	Ethnicity	Age
Avg Final Npi	1	.609**	-.495**	-.082	-.062	-.105	-.053	.080
Final GCS	.609**	1	-.724**	-.175	-.135	-.112	0	-.176*
Discharge mRS	-.495**	-.724**	1	.283**	.454**	.212**	.001	.249**
LOS	-.082	-.175*	.283**	1	.410**	.212**	.001	.249**
Discharge Location	.062	.135	.454**	.410**	1	.108	.090	.073
Sex	.105	-.112	.212**	-.092	.108	1	-.001	.062
Ethnicity	-.053	.000	.001	-.160*	.090	-.001	1	.014
Age	.080	-.176*	.249**	.042	.073	.062	.014	1

** Correlation is significant at the P = 0.01 level (2- tailed)
* Correlation is significant at the P = 0.05 level (2- tailed)

Figure 2. Correlation coefficients between patient demographic characteristics and clinical measurements

CONCLUSIONS

As we hypothesized, our results identified a strong correlation between Average Final NPi and Final GCS scores. The relationship between these two variables suggests that NPi measurements could be used similarly to GCS as an effective predictor of prognosis. Interestingly, although the three measurements (NPi, GCS, mRS) themselves displayed significant relationships, only discharge mRS exhibits a significant correlation to a patient's discharge location. Although the majority of patients were discharged home, being able to identify relationships between a patient's neurological health and inevitable discharge location could help improve hospital resource utilization and care management.

Our study also looked at whether sex, ethnicity, or age played a role in affecting the predictive capabilities of prognosis. We found that these variables had no significant associations with GCS or NPi. Finding strong correlations between certain demographic groups and the prognostic capabilities of NPi, GCS, and mRS could help make better informed decisions, however such strong demographic patterns could question the external validity of these measurement tools. These results convey that NPi and GCS can be effectively used in predicting prognosis among a potentially diverse patient demographic, although more studies are needed to confirm these findings.

Limitations of our study include the patient demographics due to the study being performed at a single institution, the clinical context of the data, and the determination of the causation or quantification of the predictive tools. Overall, future studies are needed to evaluate the potential superiority of NPi as a predictor of prognosis in multiple institutions within various neurological disease contexts.

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