Exploring the Relationship Between Objective Pupillometry Metrics and Midline Shift

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ABSTRACT

BACKGROUND: Pupillary examinations provide early subtle signs of worsening intracranial pathology. Objective pupillomtery assessment, although not yet the standard of care, is considered best practice. However, inconsistent findings from objective pupillometry studies have caused a lack of consensus among clinicians; as such, no clinical guidelines are available to guide clinical use of objective pupillometer devices. To add to the body of evidence, the purpose of this project was to explore the relationship between objective pupillometry metrics and midline shift (MLS). **METHODS:** A retrospective chart review of pupillometer data was conducted. Midline shift was correlated with objective pupillometry metrics including Neurological Pupil Index (NPi), pupil size, and anisocoria. Midline shift was measured for the patient's initial neuroimaging and with any defined neurological change. Spearman ρ was used for statistical analysis of correlations between pupillometer metrics and MLS measured at both the septum pellucidum and pineal gland. **RESULTS:** A total of 41 patients were included in the analysis; most were White (58.5%) and male (58.5%), with a mean (SD) age of 58.49 (16.92) years. Spearman ρ revealed statistically significant positive correlations between right pupil NPi and anisocoria with MLS, and significant negative correlations between left pupil NPi and pupil size with MLS. **CONCLUSIONS:** Results from this project are consistent with previous studies. Objective pupillometry continues to be a valuable component of a comprehensive neurological examination, because it has the ability to discern early and subtle changes in a patient's neurological status, leading to lifesaving interventions.

Keywords: pupillary assessment, pupillometer, device, midline shift

Neurological pupillary examinations are assessments of intracranial function and may provide subtle signs of worsening intracranial pathology hours before additional signs and symptoms become evident. Identifying these changes promptly has the ability to directly affect patient outcomes.[1] Subtle pupillary changes can signify major neurological changes. Sluggish pupillary response may represent early expanding intracranial insult or rising intracranial pressure.[2] Anisocoria (differences in right and left pupil size) may represent new or worsening intracranial pathologies.[3] Midline shift (MLS), a result of mass effect, is independently associated with poor prognosis after neurologic insult.[4,5] An MLS of 4 to 10 mm is associated with increased disability at 90 days post neurological insult via the modified Rankin score.[4,6] Lifesaving interventions can reduce morbidity and mortality from MLS; however, these must be deployed quickly.

The urgency associated with neurological changes lies within the Monro-Kellie doctrine of the cranium as a fixed space with a constant proportion of blood, brain, and cerebral spinal fluid. An increase in any 1 of the 3 components must be met with a decrease of another due to rising pressure in a contained space with potentially deadly consequences such as hydrocephalus or herniation. Insults such as cerebral edema from an acute ischemic stroke, increased volume from intracranial hemorrhage, and brain lesions increase intracranial pressure and have the capability to compress the brain away from the site of insult.[7] Accurate and reliable pupillary assessments are imperative in identifying these neurological changes promptly and accurately.[8]

Historically, pupillary assessments have been performed using subjective methods. However, studies

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have shown that subjective pupillary measurements by healthcare workers can be inconsistent and inaccurate.[2,9] When subjective and objective assessments were compared, objective pupillometry measures were more accurate than subjective assessment.[10] Anisocoria and reactivity of a pupil size of 2 mm or less proved to be highly inaccurate when assessed subjectively.[11] Objective pupillary assessment, although not yet the standard of care, is considered by numerous organizations such as the Neurocritical Care Society[12,13] and the American Association of Neuroscience Nurses[14] to be best practice and offers a portable, noninvasive assessment removing subjective inaccuracies.

The NeurOptics NPi-200 pupillometer is a commonly used device in neurocritical care units and, until recently, was the leading objective pupillometer device available in the United States. In addition to providing basic measurements of size and shape, this pupillometer quantifies pupil reactivity on a numerical scale, the Neurological Pupil Index (NPi). The Neurological Pupil Index is a proprietary measure incorporating pupillary constriction latency, constriction velocity, and dilation velocity, with ratings from 0 (nonreactive) to 4.9 (brisk); a reading of < 3 or a difference in pupil size > 0.7 mm is considered abnormal.[15]

Previous research has correlated pupillometer metrics to various neurological changes, such as intracranial pressure, MLS, and anisocoria. Taylor et al[16] found anisocoria predictive of intracranial pressure (ICP) > 30 mm Hg using objective pupillometry. Giede-Jeppe et al[17] noted patients with an NPi < 4.15 and increased ICP during objective pupillometry measurements had a 5.4% increase in ICP emergencies than participants with an NPi > 4.15. Similarly, Natzeder et al[18] found an inverse relationship between ICP and NPi exists. A recent article by Osman et al[1] found a significant correlation between horizontal shift of the septum pellucidum and NPi, but not with pupillary size in patients with ischemic stroke or intracerebral hemorrhage.

Although a growing body of research exists, inconsistent findings from objective pupillometry studies have caused a lack of consensus among clinicians.[19] As such, no clinical guidelines are available for the clinical use of objective pupillometer devices. To add to the body of evidence regarding pupillometry use, the purpose of this project was to explore the relationship between objective pupillometry metrics and MLS in the neurocritical care population.

Methods

Pupillometer data from a retrospective chart review were examined from a large neurocritical care unit in an academic health system in the southeastern United States. As a part of a level 1 trauma center and comprehensive stroke center, the unit admits adult patients with complex neurological diseases. Inclusion criteria for project participation included (1) age of 18 years or older; (2) admission to the neurocritical care unit; (3) diagnosis of stroke (ischemic, hemorrhagic, or subarachnoid hemorrhage), subdural hemorrhage, brain mass, and/or seizure; (4) an initial Glasgow Coma Scale score of 5 to 15; (5) at least 1 computed tomographic scan performed during their hospitalization; and (6) objective pupillometry metrics preserved on a patient-specific stored eye shield. This project was determined exempt by the university's institutional review board.

> Statistical significance was noted with right pupil NPi < 3 and left-to-right septum pellucidum shift.

Objective pupillometry metrics collected included right and left pupil NPi, right and left pupil size, and pupil size difference (anisocoria). Each pupillometer value was recorded once for each patient. The initial MLS was measured in millimeters to establish a baseline using the first neuroimaging scan the patient received, typically performed in the emergency department or upon admission to the neurocritical care unit. If a change in pupillary metrics or neurological status was documented in the electronic health record (defined as a Glasgow Coma Scale decrease of 2 or more points, an NPi < 3, or new-onset anisocoria), the MLS on the associated repeat neuroimaging scan was measured in millimeters. For the pupillometer metrics and MLS measurement to be included in the analyses, repeat neuroimaging scans needed to occur within a 3-hour window after the neurological changes occurred. For example, if a patient had a neurological change at 3:00 PM and a neuroimaging scan was completed no later than 6:00 PM, the MLS measured from the scan would be compared with the pupillometer metrics completed within this time frame (using the metrics measured closest to the time the scan was completed). Midline shift was measured from the septum pellucidum and the pineal gland. The first author (K.G.) assessed for MLS and performed all measurements; a second, blinded reviewer (C.B.) assessed a random sample of neuroimaging scans to validate the presence and measurements of MLS. Additional data collected included neurological diagnosis, age, sex, race, modified Rankin score, and discharge disposition.

Data Analysis

Statistical analysis was conducted using IBM SPSS version 27 with α set to .05. Spearman ρ was used to examine associations between pupillometer metrics and MLS at the septum pellucidum and pineal gland. Spearman ρ was used based on the small sample size and deviations from normality of variables. The small sample size did not allow for an adequately powered linear regression analysis. Actual values were used for pupillometer metrics and MLS measurements at both the septum pellucidum and pineal gland. Midline shift measurements were further analyzed as any shift from baseline, left to right, and right to left. Intracranial pressure monitoring values were not included in the data extraction or analysis because most participants did not have an ICP monitor in place.

Results

Patient Sample

A total of 41 patients and 66 neuroimaging scans were included. Most patients included in the sample were White (n = 24, 58.5%) and male (n = 24, 58.5%). The mean (SD) age of patients was 58.49 (16.92) years. In addition, most patients (n = 21, 51.2%) had a modified Rankin score of 6 (see Table 1). Because of the small sample size, patients were placed in 1 of 4 broad categories based on their diagnosis: stroke (ischemic, embolic, hemorrhagic, or subarachnoid; n = 29), trauma (n = 8), brain mass (n = 2), or seizures (n = 2). Patients were only included in 1 category for analysis. Of the 41 patients, 26 (56.5%) had 1 scan, and 12 (26.1%) had 2 scans, with the remaining 3 patients each having 3, 4, and 6 scans.

Relationship Between Pupillometer Metrics and MLS

Spearman ρ revealed several statistically significant correlations of MLS with abnormal NPi (<3), pupil size, and anisocoria (see Table 2). The n values reported for each correlation calculation represents the number of patients included in the analysis. Statistical significance was noted with right pupil NPi < 3 and left-to-right MLS at the septum pellucidum (n = 22, r_s = 0.47, P = .029) as well as right-to-left MLS measured at the pineal gland (n = 8, r_s = 0.72, P = .043), indicating that a higher right pupil NPi is associated with larger MLS, both left-to-right and right-to-left. A statistically significant negative correlation between an abnormal NPi measured in the left pupil and the presence of left-to-right MLS was also found (n = 8, r_s = −0.84, P = .009), indicating a lower left pupil NPi is correlated with a higher left-to-right MLS. Pupil size showed a statistical correlation to the presence of MLS measured at the pineal gland as well (left-to-right MLS: n = 8, r_s = −0.731, P = .04; right-to-left: n = 8, r_s = −0.929, P = .001). This negative correlation between pupil size and MLS indicates that, as pupil size decreased, MLS increased. Finally, statistical significance was achieved in study participants with anisocoria and left-to-right MLS measured at the pineal gland (n = 8, r_s = 0.874, P = .005), meaning that the higher the pupil size difference, the higher the left-to-right MLS.

TABLE 1. Patient Demographics (N = 41)

Variable	Descriptive Statistic
Age, mean (SD), y	58.49 (16.92)
Sex, male, n (%)	24 (58.5%)
Race, n (%)	
African American	12 (29.3)
White/Caucasian	24 (58.5)
Other	5 (12.2)
Discharge disposition, n (%)	
Home	5 (12.2)
Skilled nursing facility	8 (19.5)
Long-term acute care hospital	3 (7.3)
Death before hospital discharge	21 (51.2)
Acute rehabilitation	3 (7.3)
Hospice/palliative care	1 (2.4)
Modified Rankin score, n (%)	
2	4 (9.8)
3	4 (9.8)
4	5 (12.2)
5	7 (17.1)
6	21 (51.2)

Discussion

Our project adds to the body of literature on the relationship between objective pupillometry changes and MLS. We found statistically significant relationships between objective pupillary metrics and the presence of MLS, which is consistent with previous studies. We had a very small sample size, however, so results should be interpreted with caution. Our results are similar to Osman et al's[1] study that used data from the Establishing Normative Data for Pupillometer Assessments in Neuro-Intensive Care registry, which showed negative correlations between left pupil NPi and pupil size with MLS. Osman and colleagues[1] found a statistically significant negative correlation between right pupil NPi and MLS, which differs from our findings that showed a positive correlation. Similarly, Papangelou and colleagues[20] found that 73% of patients with transtentorial herniation had an abnormal NPi (<3) observed at some point before the herniation event. Kim et al[13] also found that patients with a significant decrease in NPi was accompanied by an aggravation of their MLS.

Accurate pupillary assessments are necessary to help identify life-threatening conditions, such as MLS. However, other clinical assessment data besides pupillometry metrics should be used to obtain a comprehensive picture of the patient's status. Further differentiation involving the outcomes for those undergoing extraventricular drains and hemicraniectomies may prove useful as a unique subset. Future studies should continue to examine the left and right pupil metrics independent of each other, because trends are poorly understood because of the lack of normative data in this population.

Implications for Nursing Practice

Objective pupillometry continues to be a valuable component of a comprehensive neurological examination because it is able to discern early, nuanced neurological changes and can help monitor worsening intracranial pathology. Nurses have a primary role in neurological assessment and contribute to the early detection of changes and potential irreversible situations.[21] Early detection allows crucial pharmacological and surgical therapies to be deployed quickly before damage or death occurs. Indeed, Anderson et al[22] found nurses reported that objective pupillometer metrics add value to patient care and critical decision-making abilities.

Bedside use of an objective pupillometer allows nursing staff to recognize subtle changes that may not be initially apparent. This early warning allows nurses to complete urgent, necessary interventions, including but not limited to notifying additional team members, administering medications, obtaining laboratory tests, and preparing for surgical intervention or neurodiagnostic testing in a timely fashion.[23]

Limitations

This project provides valuable information related to the clinical significance of objective pupillometry; however, there were several limitations. First, there was a small sample of pupillometer data available that met the inclusion criteria, limiting the generalizability of the results. This project focused on pupillary size, NPi, and anisocoria and did not account for other pupillometer metrics. In addition, this project focuses on abrupt change in level of consciousness and does not account for the gradual decline or waxing and waning of mental status; inclusion of these data could have yielded different results. Future studies on the pupillometer and clinician experiences should include larger sample sizes.

TABLE 2. Relationship Between Pupillometer Metrics and Midline Shift

Variable	Statistic	Vent Midline Shift, Right to Left	Vent Midline Shift, Left to Right	Vent Midline Shift (Any)	Pineal Midline Shift, Left to Right	Pineal Midline Shift, Right to Left	Pineal Midline Shift (Any)
R pupil NPi	n	14	**22**	37	8	**8**	37
	r_s	0.46	**0.47**	0.31	0.60	**0.72**	−0.04
	P	.09	**.029**	.06	.11	**.043**	.71
L pupil NPi	n	14	22	37	**8**	8	37
	r_s	0.34	−0.24	−0.13	**−0.84**	0.34	0.32
	P	.24	.29	.44	**.009**	.41	.06
R pupil size	n	14	22	37	**8**	**8**	37
	r_s	−0.32	−0.31	−0.21	**−0.731***	**−0.929**	0.32
	P	.26	.16	.22	**.04**	**.001**	.06
L pupil size	n	14	22	37	8	8	37
	r_s	0.13	0.22	0.11	0.32	−0.09	−0.13
	P	.66	.33	.53	.44	.82	.43
Pupil size difference (anisocoria)	n	14	22	37	**8**	8	37
	r_s	0.25	0.38	0.23	**0.874**	0.59	−0.32
	P	*.40*	*.08*	*.18*	**.005**	*.12*	*.06*

Note. Spearman ρ was used based on the small sample size and deviations from normality of variables (Shapiro-Wilk's *P* values < .05 for vent shift R to L, vent shift L to R, GCS, R pupil NPi, any vent shift, and any pineal shift). L, left; NPi, Neurological Pupil Index; R, right. Data in bold indicates statistically significant findings.

Conclusion

This project explored the relationship between objective pupillometry metrics and MLS. Statistically significant relationships were identified, and this study adds to the growing body of literature focused on objective pupillary metric use in critically ill neuroscience patients. Objective pupillometry has the ability to discern early and subtle changes in a patient's neurological status. Its use may be potentially lifesaving and is vital to a comprehensive bedside neurological assessment.

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