Diagnostic Value of Point-of-Care Ultrasound-Guided Assessment of Relative Afferent Pupillary Defect in Adult Ocular Trauma Patients Presenting to the Emergency Department

A Prospective Cohort Study

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Abbreviations

ATLS, Advanced Trauma Life Support; CI, confidence interval; ED, emergency department; EM, emergency medicine; NPV, negative predictive value; POCUS, point-of-care ultrasound; PPV, positive predictive value; RAPD, relative afferent pupillary defect; TBI, traumatic brain injury

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Objectives—Early diagnosis of relative afferent pupillary defects (RAPDs) in patients with ocular trauma is crucial for timely management and improved outcomes. However, clinical examination can be challenging for patients with periorbital ecchymosis. This study aimed to compare the diagnostic accuracy of point-of-care ultrasound (POCUS) and clinical examination by emergency physicians for detecting RAPD in adult ocular trauma patients and to evaluate the proportion of RAPD in patients with ocular trauma who presented to the ED.

Methods—This prospective cohort study was conducted at an academic emergency department in South India. Adult ocular trauma patients were assessed for RAPD using clinical examinations by emergency physicians and POCUS. The diagnostic accuracies of both methods were compared, with the ophthalmologist's final diagnosis serving as the gold standard. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both techniques.

Results—A total of 376 patients (median age, 35 years) were included in this study. RAPD was identified in 14.63% of the patients. The sensitivity and specificity of POCUS in detecting RAPD were 92.73% and 99.38%, respectively, which were higher than those of clinical examination, with a sensitivity of 81.82% and specificity of 99.07%. The PPV and NPV of the clinical examination were 93.75% and 96.95%, respectively, whereas the PPV and NPV of POCUS were 96.23% and 98.76%, respectively. POCUS accurately diagnosed RAPD in patients with periorbital ecchymosis.

Conclusion—POCUS-guided RAPD assessment proves to be a better diagnostic adjunct compared to clinical examination in patients with ocular trauma presenting to the emergency department.

Key Words—emergency medicine; ocular trauma; point-of-care testing: ultrasonography; pupillary reflex; relative afferent pupillary defect

Ocular trauma is a significant cause of visual impairment worldwide, with the World Health Organization reporting that 55 million people experience serious ocular trauma annually.[1] In certain regions, ocular trauma accounts for up to 2.4% of cases of blindness.[2] One of the consequences of ocular trauma is the relative afferent pupillary defect (RAPD), a condition in which pupils respond asymmetrically to light due to unilateral or asymmetric retinal or optic nerve disease. Detecting of RAPD will help in early diagnosis of traumatic optic neuropathy which are often missed during initial management of polytrauma and patients with altered mental status. However, detecting and measuring RAPD can be difficult, especially when the patient has periorbital ecchymosis that obscures the view of the pupil. Identifying and accurately quantifying RAPD in ocular injuries is challenging due to examiner bias, light location variability, and endpoint selection, among other factors. Delayed diagnosis of optic nerve damage can result in permanent vision loss. Recent research has found an inter-examiner disagreement as high as 39% in manual pupillary response assessment, highlighting the need for an objective RAPD evaluation method.[3] Various methods have been described for quantifying or assessing RAPD, including neutral density filters, cross-polarized filters, and subjective grading based on the initial pupil contraction and subsequent dilation as light swings.[4–6] Although effective and accurate, these approaches are influenced by factors that affect their validity, variability, and reliability. Unfortunately, these endpoints remain subjective despite objective measurements.

Point-of-care ultrasonography (POCUS) is a portable, noninvasive imaging technique that has been used to accurately identify internal ocular injuries, such as iris injury, vitreous hemorrhage, retinal detachment, and lens dislocation, even in the presence of periorbital ecchymosis. While POCUS has the potential to objectively measure pupillary diameter, its utility and diagnostic value in assessing pupillary reflexes and RAPD in emergency settings have yet to be fully explored.[7] To date, the only study examining the use of ultrasound to detect RAPD has introduced it as a novel, objective method but fell short of measuring its diagnostic utility comprehensively.[8] Therefore, our study aimed to fill this gap by determining the diagnostic utility of POCUS for subjectively assessing the presence of RAPD in patients with ocular injuries presenting to the emergency department (ED).

Methods

Study Design and Time Period

We conducted a single-center prospective cohort study. Data were collected prospectively by an emergency physician between May 2020 and July 2022, using a convenient sampling method to enroll patients. Ethical approval for this study was obtained from the institutional ethics committee and was conducted in accordance with the Declaration of Helsinki. The STARD 2015 guidelines for reporting diagnostic accuracy studies were used in the preparation of the manuscript.

Study Setting

This study was conducted in the ED of the Jawaharlal Institute of Postgraduate Medical Education & Research, a tertiary care academic ED in South India that receives 60,000 patients annually.

Study Population

All adult ocular trauma patients aged >18 years were included in this study after obtaining written informed consent. Patients with suspected open globe injury and polytrauma who required immediate surgery as part of their resuscitation, those using topical medication that affects pupillary function, and those who had a history of ocular diseases such as glaucoma, macular degeneration, diabetic retinopathy, pontine hemorrhage, or traumatic mydriasis were excluded from this study.

Intervention

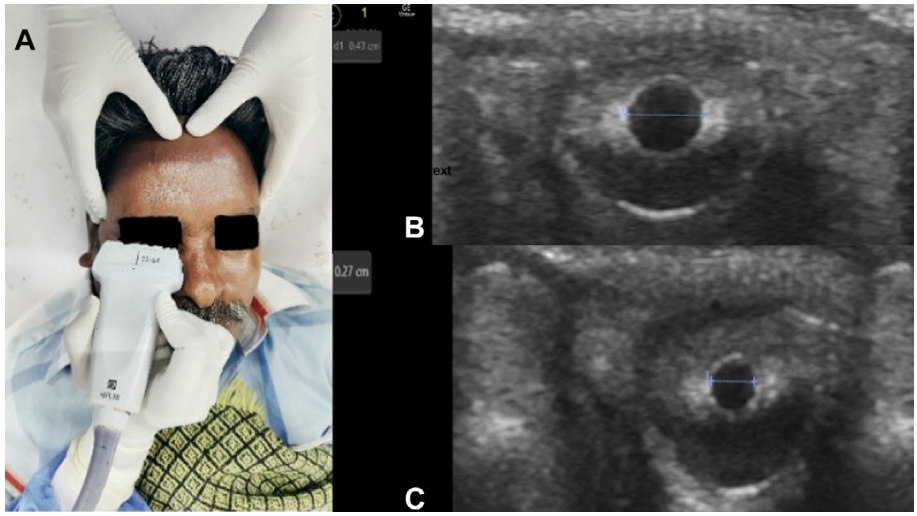
Patients who had sustained ocular trauma and presented during the trained EP shift were enrolled in the study after obtaining written informed consent from them or their relatives. Upon arrival at the ED, patients underwent an initial assessment and stabilization according to standard treatment protocols by the treating EP or resident. Subsequently, they performed a routine clinical examination, which included a

swinging flashlight test of both eyes. All POCUS assessments were performed by a single EP who had undergone specific training on the technique and was unaware of the treating team's diagnosis. This EP received hands-on training from a POCUS-trained and credentialed EP in 30 ocular scans before the commencement of the study, ensuring he was proficient in POCUS-guided RAPD assessment in 3–5 minutes. Patients were examined in the supine position, and the examiner positioned themselves at the patient's head end. The POCUS examination was performed using the Venue-Go ultrasound system, equipped with a 7–12 MHz linear array transducer, set to superficial depth settings, in compliance with established guidelines for orbital sonography and employing the ALARA (as low as reasonably achievable) principle to minimize radiation exposure. The probe was placed flat on the lower eyelid at a 45° angle from the globe of the eye, with a depth setting of 1.8 cm, utilizing a closed-eye technique and applying a water-soluble gel (Figure 1). The pupillary size was measured in the resting position, and the pupils' response to the light stimulus was digitally documented for both eyes using a standard penlight with a luminous emittance of 70,000 Lux and a stimulus time of 2 seconds (Figure 1). The assessment process was consistent for all patients, starting with measuring the right eye's pupillary diameter at rest, during ipsilateral and contralateral light stimulation, and then proceeding with the left eye's tests in the same manner (Figure 2). All the POCUS images were saved and reviewed by a POCUS-trained and credentialed EP, who was also blinded to ophthalmologist's examination. All patients with ocular trauma were subsequently evaluated within 1 hour by a board-certified ophthalmologist on duty at the bedside, and their final diagnosis of RAPD served as the gold standard. In all cases, the ophthalmologists were blinded to the study sonographers findings. The clinical findings from routine examination and ocular POCUS findings were collected and compared to determine the effectiveness of POCUS in identifying RAPD.

Outcome Measures

The primary outcome was to determine the diagnostic accuracy of POCUS-guided assessment of RAPD and clinical examination by the EP, compared with the examination by an ophthalmologist as the gold standard in adult ocular trauma presented to the ED. The secondary outcome was to determine the proportion of RAPD in patients with ocular trauma who presented to the ED.

Figure 1. A, Assessment of pupillary reactions by POCUS. **A**, Position of the ultrasound probe (7–12-MHz linear array transducer in transverse orientation). Pupillary diameter assessment in the closed eye by POCUS. **B** and **C**, Example of pupillary diameter (PD) assessment in the closed eye by the POCUS. **B**, PD at rest. **C**, PD during light reflex. Crosses represent the marker set by the examiner for measuring the PD.



Data Analysis

The collected data were tabulated using Microsoft Excel and analyzed using the SPSS software (IBM SPSS Statistics version 19.0). Continuous variables, such as age, systolic blood pressure, diastolic blood pressure, pulse rate, oxygen saturation, and pupillary diameter, were summarized as either mean with standard deviation or median with interquartile range based on normality. Categorical variables, such as sex, comorbidities, mode of injury, type of ocular injury, and the presence of RAPD, were expressed as frequencies or percentages. The diagnostic accuracy of POCUS in detecting RAPD compared with clinical assessment was measured by calculating the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio. The kappa coefficient was also used to measure the level of agreement between the clinical examination and gold standard diagnosis and to measure the level of agreement between POCUS and gold standard diagnosis.

Sample Size

The sample size was determined using nMaster 2.0 software, with a 25% incidence of RAPD in ocular trauma cases, based on a study by Serdarevic, given the innovative nature of the diagnostic tool and absence of prior data on its sensitivity a 50% sensitivity rate was assumed for point-of-care ultrasound in diagnosing RAPD, a 95% confidence interval (CI), power of 80%, and a 5% alpha error.[9] The required number of RAPD cases for the study was 94. Considering a 25% incidence of RAPD among ocular trauma cases, 376 ocular trauma cases were screened.

Results

Baseline Characteristics

Of the 413 patients with ocular trauma who were approached for enrolment, 13 had clinically obvious open globe injury, 18 did not consent, and 6 patients required immediate surgical intervention. Three

Figure 2. POCUS-guided pupillary assessment for diagnosing RAPD. Step 1: Pupillary diameter at resting state of right eye. Step 2: Pupillary diameter at resting state left eye. Step 3: Pupillary size of the right eye when light is shone on the right eye (direct light reflex). Step 4: Pupillary size of the right eye when the light is shone on the left eye (indirect light reflex of right eye). Step 5: Left eye when the light is shone to the left eye (direct light reflex of the left eye). Step 6: Pupillary size of the left eye when the light is shone on the right eye (indirect light reflex of the left eye).

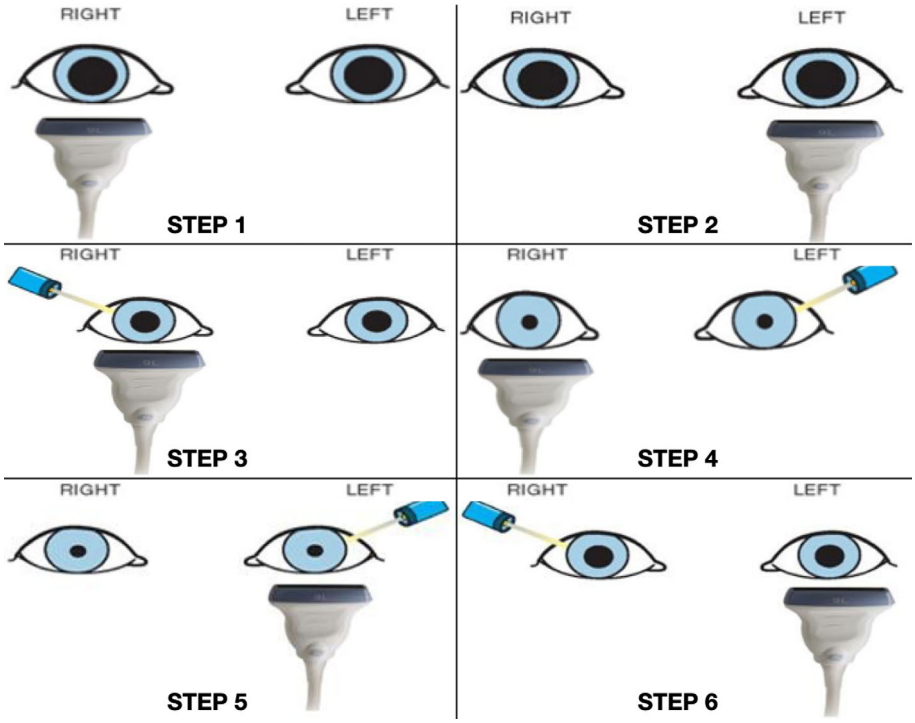


Table 1. Baseline Characteristics, Vital Signs, Neurological Status, Ocular Injury Types, Pupillary Diameter Assessment, and RAPD Diagnosis Among Adult Ocular Trauma Patients (n = 376)

Characteristic	Frequency
Gender, n (%)	
Male	334 (88.8)
Female	42 (11.2)
Comorbidities, n (%)	
Diabetes mellitus	13 (3.5)
Hypertension	17 (4.5)
Both	4 (1.1)
None	342 (90.9)
Mode of injury, n (%)	
Road traffic accident	226 (60)
Fall from standing	113 (30)
Assault	30 (8)
Fall from height	7 (2)
Severity of TBI, n (%)	
Mild TBI (GCS 13–15)	275 (73.1)
Moderate TBI (GCS 9–12)	70 (18.7)
Severe TBI (GCS 3–9)	31 (8.2)
Type of ocular injury, n (%)	
Ecchymosis	316 (84)
Laceration	24 (6.4)
Subconjunctival hemorrhage	71 (18.9)
Hyphema	32 (8.5)
Pupillary diameter assessment, median (IQR)	
Right eye at rest	3.0 (3.0–4.0)
Left eye at rest	3.0 (3.0–4.0)
Right eye on direct light reflex	2.0 (2.0–3.0)
Left eye on direct light reflex	2.0 (2.0–2.0)
Right eye on indirect light reflex	2.0 (2.0–3.0)
Left eye on indirect light reflex	2.0 (2.0–2.0)
RAPD diagnosis, n (%)	
Present	55 (14.6)
Absent	321 (85.4)

GCS, Glassgow Coma Scale; IQR, interquartile range.

hundred and seventy six adult ocular trauma patients met the inclusion criteria, with a male predominance (88.8%) and a mean age of 38.77 ± 12.85 years. Patients aged 26–40 years represented the largest age group. Common comorbidities included diabetes mellitus (3.5%) and hypertension (4.5%). Road traffic accidents constituted the primary cause of ocular trauma (60%), followed by falls from standing (30%), assaults (8%), and falls from heights (2%). Most patients experienced mild traumatic brain injury (TBI) (73.1%), while moderate and severe TBI occurred in 18.7% and 8.2% of patients, respectively (Table 1).

Primary Outcome

POCUS demonstrated a sensitivity of 92.73% (95% CI: 82.41–97.98), specificity of 99.38% (95% CI: 97.77–99.92), positive predictive value of 96.23%, negative predictive value of 98.76%, positive likelihood ratio of 148.83, negative likelihood ratio of 0.07, and accuracy of 98.40% (95% CI: 96.56–99.41) in detecting RAPD compared to clinical examination alone (sensitivity: 81.82%; 95% CI: 69.10–90.92; specificity: 99.07%; 95% CI: 97.29–99.81; positive predictive value: 93.75%; negative predictive value: 96.95%; positive likelihood ratio 87.55; negative likelihood ratio: 0.18; accuracy: 96.54%; 95% CI: 94.16–98.15) (Table 2,3).

Secondary Outcome

Approximately 15% of adult patients with ocular trauma (n = 376) had RAPD, as determined by the gold standard examination performed by ophthalmologists.

Table 2. Primary Outcome and Subgroup Analysis: Diagnostic Accuracy and Agreement of POCUS and Clinical Examination for RAPD Detection Among Adult Ocular Trauma Patients (n = 376)

Parameter	POCUS	Clinical Examination
Diagnostic accuracy		
Sensitivity (%)	92.73 (95% CI: 82.41–97.98)	81.82 (95% CI: 69.10–90.92)
Specificity (%)	99.38 (95% CI: 97.77–99.92)	99.07 (95% CI: 97.29–99.81)
Positive likelihood ratio	148.83 (95% CI: 37.31–593.70)	87.55 (95% CI: 28.19–271.87)
Negative likelihood ratio	0.07 (95% CI: 0.03–0.19)	0.18 (95% CI: 0.10–0.32)
Positive predictive value (%)	96.23 (95% CI: 86.47–99.03)	93.75 (95% CI: 82.85–97.90)
Negative predictive value (%)	98.76 (95% CI: 96.88–99.51)	96.95 (95% CI: 94.78–98.24)
Accuracy (%)	98.40 (95% CI: 96.56–99.41)	96.54 (95% CI: 94.16–98.15)
Agreement with gold standard		
Agreement (%)	95.6	86.4
Kappa (κ)	0.956 ($P < .001$)	0.864 ($P < .001$)

Subgroup Analysis

The agreement between POCUS performed by emergency medicine (EM) physicians and the gold standard examination by ophthalmologists for RAPD detection was almost perfect (95.6%; $\kappa = 0.956$, $P < .001$). Conversely, the agreement between the clinical examination by emergency physicians and the gold standard examination demonstrated a strong level of agreement (86.4%; $\kappa = 0.864$, $P < .00$) (Table 2).

Discussion

In this prospective study, we evaluated the diagnostic accuracy of clinical examination and POCUS performed by EM physicians to detect RAPD in ocular trauma patients. Our results demonstrated high specificity and positive predictive value for both methods, with POCUS exhibiting improved sensitivity and negative predictive value compared with clinical examination. These findings suggest that POCUS has the potential to enhance RAPD detection in ocular trauma patients and reduce the rate of false-negative results. The high level of agreement between POCUS performed by EM physicians and the gold standard examination by ophthalmologists ($\kappa = 0.956$, $P < .001$) highlights the reliability and reproducibility of POCUS in detecting RAPD. In comparison, clinical examination showed a strong yet lesser degree of agreement with the gold standard examination ($\kappa = 0.864$, $P < .001$). This finding underscores the benefits of incorporating POCUS into the diagnostic workflow for adult ocular trauma patients, potentially leading to expedited management and better clinical outcomes. While POCUS-guided RAPD assessment demonstrated higher sensitivity, potentially leading to rapid detection of RAPD and thereby improving patient management and outcomes, it is important to recognize that clinical examination, despite its slightly lower sensitivity, may still be sufficient in certain contexts, particularly in settings where POCUS is unavailable. Our study also revealed a higher prevalence of ocular trauma in males and younger individuals, with road traffic accidents as the leading cause of injury. Additionally, we found that around 15% of adult ocular trauma patients had RAPD, highlighting the need for accurate RAPD detection, as it can indicate optic nerve dysfunction, retinal injury, or other severe ocular pathologies, warranting prompt intervention.

Our findings concur with those of prior studies that reported a higher incidence of ocular trauma in males and younger populations.[2,10–12] Road traffic accidents emerged as the predominant cause of injury in our study, followed by falls under the influence of alcohol, assault, and falls from heights. These results align with those of Koval[10] and Cillino et al, who identified road traffic accidents and assaults as the leading causes of ocular trauma.[13] In contrast, other studies from India have reported different injury mechanisms such as firecrackers, household objects, and agricultural tools.[14,15] We observed RAPD in 15% of our patients, a higher rate than the global incidence of RAPD (ranging from 0.7% to 2.5%), as reported in studies from the UK and Glasgow.[16,17] This discrepancy may be attributable to the high frequency of road traffic accidents in India, poor adherence to traffic regulations, and helmet use among two-wheel drivers. Our findings are consistent with those of a study by Singh et al in AIIMS Delhi, which reported RAPD in 12.4% of ocular trauma patients.[18] We subjectively assessed the median pupillary diameter at rest and found it smaller than the mean pupillary diameter reported in other

Table 3. Comparison of Point of Care Ultrasound (POCUS) Done by Emergency Physician (EP) and Clinical Examination Done by EP for Assessment of RAPD With Gold Standard (Ophthalmologist) Diagnosis

	RAPD by Ophthalmologist (Gold Standard)		
Assessment Method	**RAPD, n = 55**	**No RAPD, n = 321**	**Total, n = 376**
Clinical Examination by EP	True positive (45)	False positive (3)	48
	False negative (10)	True negative (318)	328
POCUS by EP	True positive (51)	False positive (2)	53
	False negative (4)	True negative (319)	323

studies.[19,20] This difference could be due to variations in the lighting conditions in a busy ED where maintaining a dark environment for patients was logistically challenging.

The use of B-mode ultrasound for detecting RAPDs was first introduced by Schmidt et al in a study involving 17 patients with nontraumatic optic neuropathy, where they reported its effectiveness in providing a quick, easy, well-tolerated, and objective approach for quantifying and digitally recording RAPD.[8] To the best of our knowledge, this is the first study comparing the diagnostic accuracy of RAPD detection using clinical examination and POCUS conducted by EM physicians in ocular trauma patients. Prior studies have employed alternative diagnostic tools, such as infrared pupilometers and automated pupilometers, which demonstrated lower sensitivity and specificity than POCUS when compared to clinical diagnoses by ophthalmologists or healthy controls.[21,22] These devices may not be practical for patients with ocular trauma who struggle to open their eyelids or sit up and may necessitate additional space and equipment in a crowded ED. In contrast, POCUS has already been integrated into trauma resuscitation protocols and can be conveniently performed at the bedside. Literature reveals a high level of interest among EM physicians in the use of POCUS globally, and in India, availability of these has been made mandatory in the ED by the medical council.[23–26] Advanced Trauma Life Support (ATLS) guidelines already endorse the use of E-FAST (Extended Focused Assessment with Sonography for Trauma) during trauma resuscitation in ED. By extending the application of POCUS to include the assessment of traumatic injuries, such as traumatic optic neuropathy through RAPD assessment, fracture detection and optic nerve sheath diameter for detecting raise intracranial pressure, rapid diagnosis could be further facilitated. Integrating this to the ATLS training program could even address the potential learning curve associated with its use in ED.

POCUS-guided pupillary assessment is noninvasive, cost-effective, and enables real-time visualization. Moreover, POCUS allowed accurate real-time measurement of pupillary changes when assessing RAPD, which could prove valuable in fast-paced emergency settings. Importantly, POCUS accurately detected RAPD in patients with periorbital ecchymosis. In patients with periorbital ecchymosis, traditional pupillary assessment usually requires manual or speculum-assisted opening of edematous eyelids, which can cause significant pain and discomfort. In contrast, our study found that POCUS-guided RAPD assessment, employed on most patients with ecchymosis, resulted in considerably less discomfort and pain during evaluation compared to these conventional clinical assessments. Although we did not quantitatively measure the pain score and patient satisfaction, this marked reduction in patient discomfort was a significant observation in our study. This finding suggests that POCUS-guided RAPD assessment could replace clinical assessment, warranting further investigation in future studies.

Our study has several limitations, including its single-center, nonrandomized design and inclusion of only patients aged >18 years. The convenience sampling method would have introduced selection bias. Only a small number of providers (1 EP and 4 ophthalmologists) were involved in the evaluation of patients in this study. The study sonographer received extensive training before the study, limiting the external validity of our findings. POCUS-guided pupillary measurement, although exhibiting a steep learning curve, remains operator-dependent, with reliability and accuracy contingent on the operator's experience. Minor variations in light settings inherent to the ED might have affected pupillary light reflex assessment. Additionally, data were not recorded regarding which EP's performed the clinical examination and which ophthalmologist performed each RAPD assessment, thus precluding the determination of interrater reliability. Consequently, potential variability in the gold standard diagnoses due to the involvement of multiple ophthalmologists could have influenced the Kappa agreement values. Our study's findings may be influenced by the high prevalence of alcohol consumption and head injuries in our region, potentially confounding RAPD detection and limiting generalizability due to specific demographic and regional characteristics. Our study's limitations also include the absence of follow-up clinical outcomes for RAPD-diagnosed patients, leaving the impact of POCUS on treatment decisions and expedited ophthalmologist evaluation unexplored, which future studies should consider investigating.

Finally, our sample size calculation relied on a 25% incidence of RAPD derived from the Serdarevic study, which was conducted in an ophthalmology department.[9] This setting, specialized in ocular cases, could potentially see a higher rate of RAPD incidences than an ED due to the nature and severity of injuries presented. Consequently, this might have led to an overestimation of RAPD incidence during sample size calculation for our study, which was conducted in an ED setting. This could potentially impact the overall accuracy estimate, though it is unlikely to affect the sensitivity, specificity, and comparison between the methods. It is essential to note the assumption made regarding the 50% sensitivity of the new diagnostic tool for RAPD. This assumption was necessary due to the lack of existing data on the tool's sensitivity and is a common practice in studies involving novel diagnostic methods. Notably, the actual sensitivity observed in our study exceeded the initial assumption, which, in turn, would have only served to increase the study's power. Future research, utilizing the preliminary data collected from this study will help in further refining our understanding and application of this diagnostic method in ED settings.

POCUS-guided RAPD assessment presents a noninvasive, cost-effective, and accurate approach in contrast to conventional clinical evaluation for adult ocular trauma patients, especially in cases with periorbital ecchymosis. Future research should validate these findings across diverse populations and geographic locations, explore the potential of artificial intelligence-assisted pupillary diameter measurements, and address limitations such as operator dependence and variations in ambient light conditions.

Conclusion

Point-of-care ultrasound for detection of RAPD in ocular trauma patients performed by an emergency physician had high sensitivity, specificity, and better accuracy than clinical examination. POCUS-guided RAPD was in almost perfect agreement with the gold standard diagnosis by an ophthalmologist. Future studies can explore the utility of POCUS in more diverse populations.

Ethics Approval

This study has received ethics approval from the Jawaharlal Institute of Postgraduate Medical Education and Research, Institute Ethics Committee.

Consent to Participate

Informed written consent was taken from every study participant.

Consent for Publication

All authors consent to publication.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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