

## Introduction

- TBI is a major cause of death and disability in the USA
- Poor pupil reactivity has been shown to be an early predictor of neurological deterioration<sup>1</sup>
- Absent pupil reactivity can help stratify severity and prognosticate outcome<sup>2</sup>
- Abnormal pupil phenotypes over the first 72 hrs in mild, moderate, and severe TBI patients is poorly characterized

## Objectives

- Calculate the incidence and burden of abnormal pupil phenotypes including unilateral and bilateral pupil deficits
- Investigate the relationship of abnormal pupil phenotypes and unfavorable outcomes at discharge

## Methods

- A single-center retrospective observational study of 136 TBI patients in the Neuro ICU from 2018-2022 with quantitative pupil measurements in the first 72 hours using the Neuroptics pupillometer

	Overall (n=136)	Mild TBI (n=49)	Moderate TBI (n=20)	Severe TBI (n=67)	p-value
<b>Demographics</b>					
Age (years), median [Q1, Q3]	58 [38,71]	66 [60,80]	54 [45,75]	48 [28,64]	<0.001
Sex Male, n (%)	96 (71)	34 (69)	10 (50)	52 (78)	0.058
<b>Race, n (%)</b>					
White	73 (54)	30 (61)	11 (55)	32 (48)	0.109
Black	28 (21)	8 (16)	4 (20)	16 (24)	
Hispanic	14 (10)	6 (12)	1 (5)	7 (10)	
Other	5 (4)	4 (8)		1 (2)	
Unknown	16 (12)	1 (2)	4 (20)	11 (16)	
Glasgow Coma Scale on Admission, median [Q1, Q3]	9 [6,14]	15 [14,15]	10 [10,11]	6 [3,7]	<0.001
<b>Mechanism of Injury, n (%)</b>					
Blunt	127 (93)	46 (98)	19 (95)	60 (90)	0.189
Penetrating (GSW)	9 (7)	1 (2)	1 (5)	7 (10)	
ICP Monitor, n (%)	18 (13)	2 (4)	2 (10)	16 (24)	0.001
EVD Placement, n (%)	26 (19)	8 (16)	4 (20)	14 (21)	0.821
Decompressive Surgery, n (%)	30 (22)	9 (18)	4 (20)	17 (25)	0.649
Marshall CT Score, median [Q1, Q3]	2 [2,5]	2 [2,5]	2 [2,5]	3 [2,5]	0.349
Rotterdam CT Score, median [Q1, Q3]	2 [2,3]	2 [2,3]	2 [2,3]	3 [2,4]	0.002

Table 1: Characteristics of study cohort

- Patients with pre-existing eye conditions were excluded
- TBI patients were stratified by severity based on GCS

## Definitions

- Poor pupil reactivity: neurological pupillary index (NPi) < 3
- Asymmetric pupil reactivity: difference in NPi ≥ 0.7
- Anisocoria: size difference in eyes > 1

### Categories of Pupil Abnormalities

Category	Definition
Any	Unilateral or bilateral NPi < 3, Diff NPi ≥ 0.7, or Diff Size > 1
Unilateral	Unilateral NPi < 3, Diff NPi ≥ 0.7, or Diff Size > 1
Bilateral	Bilateral NPi < 3

Table 2: Definitions for each category of abnormal pupil phenotypes

- Burden =  $\frac{\text{total number of observations where stage criteria met}}{\text{total number of observations}}$
- Unfavorable Outcomes: discharge disposition of deceased, hospice, or long-term care

## Results

### Visualization of Pupil Trajectories

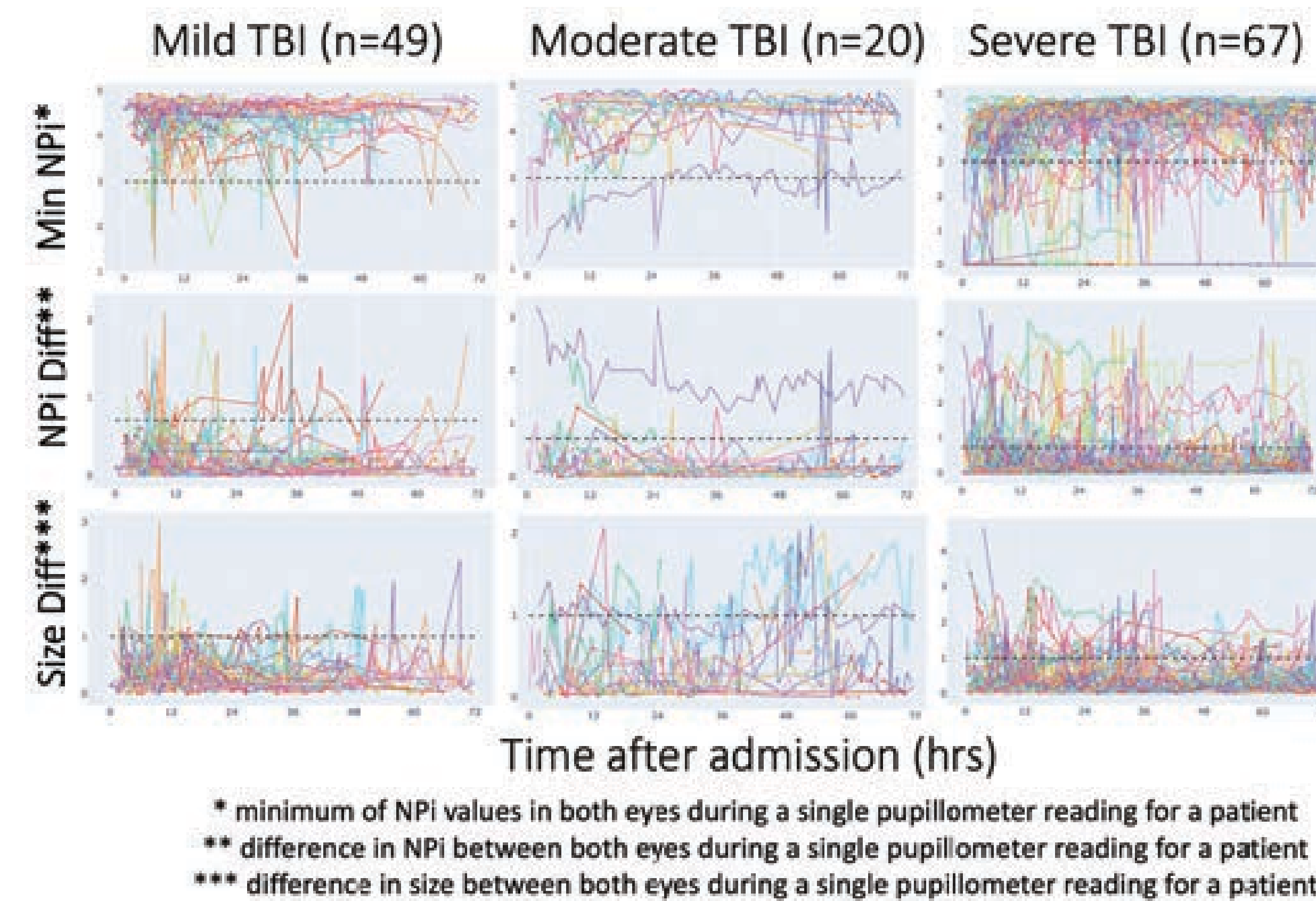


Figure 1: Trajectories of pupil NPi, minimum NPi, and size difference over the first 72 hours from admission for TBI patients show increased pupil abnormalities (NPi < 3, Diff NPi ≥ 0.7, or Diff Size > 1 with thresholds displayed as black dashed line) between patients with mild and severe TBI

## Predicting Unfavorable Outcomes using Logistic Regression

A) Incidence of Pupil Abnormality				B) Burden of Pupil Abnormality			
Pupil Abn	OR	95% CI	p val	Pupil Abn	OR	95% CI	p val
Any	1.45	0.49-4.67	0.5	Any*	1.03	1.01-1.05	0.004
Unilateral	1.12	0.40-3.27	0.8	Unilateral	1.02	1.00-1.04	0.12
Bilateral*	6.65	2.07-23.7	0.002	Bilateral*	1.19	1.05-1.41	0.02

Table 3: Logistic regression results for incidence and burden of each pupil abnormality on unfavorable outcomes in patients (\* = statistical significance)

## Predicting Survival in TBI Patients using Cox proportional-hazards model

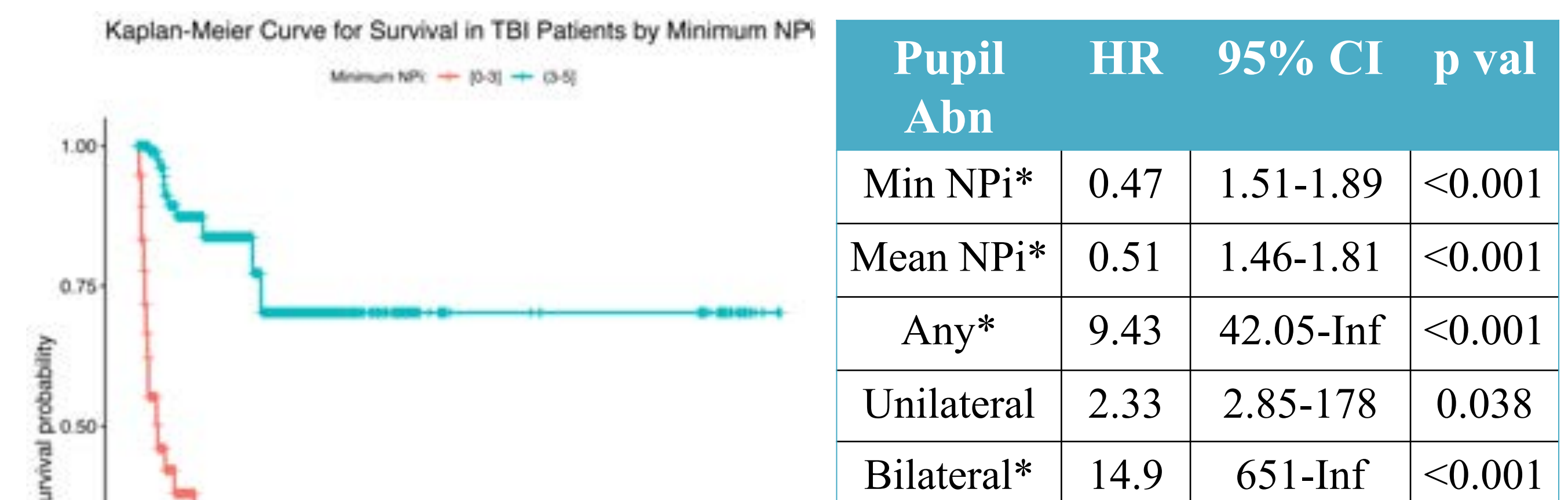


Table 4: Hazard ratios for pupil abnormalities (\* = statistical significance)

Figure 2: Kaplan-Meier Curve for Survival by Minimum NPi

## Conclusions

- Incidence and burden of bilateral nonreactive pupils in the first 72 hours is associated with unfavorable outcomes in TBI patients
- Burden, not incidence, of any pupil abnormality is associated with unfavorable outcomes in TBI patients
- Unilateral pupil abnormalities are not associated with unfavorable outcomes
- Many pupil abnormalities are associated with mortality

## References

- Chesnut, R.M.; Gauttill, T.; Blunt, B.A.; Klauber, M.R.; Marshall, L.E. The Localizing Value of Asymmetry in Pupillary Size in Severe Head Injury: Relation to Lesion Type and Location. *Neurosurgery* 1994, 34, 840-845; discussion 845-846.
- Romagnosi, F.; Bernini, A.; Bongiovanni, F.; Iaquaniello, C.; Miroz, J.-P.; Citerio, G.; Taccone, F.S.; Oddo, M. Neurological Pupil Index for the Early Prediction of Outcome in Severe Acute Brain Injury Patients. *Brain Sci.* 2022, 12, 609. <https://doi.org/10.3390/brainsci12050609>