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OPTIC NERVE SHEATH DIAMETER ON CT BRAIN AS A PREDICTOR OF MORBIDITY AND MORTALITY IN PATIENTS WITH TRAUMATIC BRAIN INJURY

By

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A research report submitted in fulfilment of the requirements for the degree of

Masters of Medicine in Neurological Surgery

In the

Faculty of Health Sciences

University of the Witwatersrand



Johannesburg, 2016

DECLARATION

I, Dr Motlhabane Madumo, declare that the research report that I hereby submit for the degree of Masters of Medicine in Neurological Surgery at the University of the Witwatersrand is my own work. The research report has not been submitted by me for any other degree or examination at this or any other university. The study will be submitted for publication.

……

DEDICATION

This research report is dedicated to:

The Lord, through whom all things are possible.

My wife, Pontsho and my children who have been patient, encouraging and supportive through all the challenges in my career defining journey.

I want to thank my parents, Ellen Mmakuba and the late Isaac Sokhahlwayini Madumo for the guidance and the sacrifices they made to ensure that all their children had better opportunities as well as their efforts to bring out the best in all of us.

To all my colleagues for their meaningful contribution, support and motivation throughout this journey.

ABSTRACT

Background: Traumatic Brain Injury (TBI) is very common in our setting and puts a strain on the healthcare system and social welfare services. There are no formal statistics reported locally, however we treat many patients with TBI due to assaults, motor vehicle accidents (MVA) and falls at the two major hospitals in Johannesburg. TBI is a common cause of major disability and loss of income among young and middle aged South Africans. The development of a reliable prognostic factor in addition to existing ones would help guide therapy and allow prioritization of resources for TBI patients. Other studies have demonstrated the direct correlation between measured Intracranial pressure (ICP) and Optic Nerve Sheath Diameter (ONSD), however there is no consensus regarding the normal ONSD. ONSD varies in children, adults and among different populations.

Objectives: Establish an average ONSD among adult patients presenting at Chris Hani Baragwanath Academic Hospital and Charlotte Maxeke Johannesburg Academic Hospital. To measure the ONSD on CT brain and correlate with outcome upon discharge or thirty days (whichever comes first) in adult patients with severe traumatic brain injury in our setting using a Glasgow Outcome Scale (GOS) score.

Methods: We conducted a prospective observational study from July to December 2015 at two major hospitals with neurosurgical facilities in Johannesburg. Study subjects were adult male and female patients (>18yrs) with severe TBI as well as adult patients with normal scans performed within the study period (Controls).

Results: 40 severe TBI patients and 42 controls were enrolled in the study. Most patients in the study were young adult males (n=37) who sustained their injuries due to assaults (43%) and MVA/PVA (28%). Admission GCS had 3 categories, with the majority of patients in the GCS category 3 (45%). ONSD average in normal subjects was 5.36mm, while in TBI patients the average ONSD was 5.6mm. There were 12 deaths, 18 patients with poor outcome and 10 patients with good outcome.

Conclusion: Our results showed that the ONSD is not a reliable prognosticator in severe TBI patients. The ONSD correlation with GOS and Rotterdam score was not statistically significant with a p-values of 0.096 and 0.876 respectively.

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TABLE OF CONTENTS

Item	Content	Page
	Title page	i
	Declaration	ii
	Dedication	iii
	Abstract	iv
	Acknowledgements	v
	Table of contents	vi
	List of figures	viii
	List of tables	ix
	List of abbreviations	x
	Chapter 1	
1.1	Introduction	1
1.2	Literature review	3
1.3	Justification of the study	5
1.4	Study objectives	5
	Chapter 2: METHODS	
2.1	Research design	6
2.2	Study period and setting	6
2.3	Patient selection	6
2.3.1	Inclusion criteria	6
2.3.2	Exclusion criteria	6
2.3.3	Limitations	7
2.3.4	Measurements	7
2.3.5	Data analysis	8
	Chapter 3	
3.1	Results	9
	Chapter 4	
4.1	Discussion	19

	Chapter 5	
5.1	Conclusion	20
	Appendix A: Ethics approval letter	
	Appendix B: Consent form	
	Appendix C: Data collection form	
	Appendix D: Rotterdam score	
	Appendix E: Glasgow Outcome Scale	
	References	21

LIST OF FIGURES

Figure	Description	Page
2.3.4.1	Optic Nerve Sheath Diameter measurement on CT scan	7
3.1	Age range	10
3.2	Gender distribution	10
3.3	Mechanism of injury	11
3.4	GCS	11
3.5	Rotterdam Score	12
3.6	Control Optic nerve sheath diameter	13
3.7	Optic nerve sheath diameter in TBI patients	14
3.8	ONSD vs Rotterdam score vs GOS	15
3.9	Glasgow Outcome Scale score results	16

LIST OF TABLES

Table no	Description	Page
3.1	ONSD vs Rotterdam as predictors of outcome	17
3.2	ONSD as a predictor of outcome	17
3.3	ONSD and Rotterdam correlation	18

List of Abbreviations:

CHBAH - *Chris Hani Baragwanath Academic Hospital*

CMJAH - *Charlotte Maxeke Johannesburg Academic Hospital*

CI - *Confidence Interval*

CNS - *Central Nervous System*

CSF - *Cerebral Spinal Fluid*

CTB - *Computed Tomography of the Brain*

GCS - *Glasgow Coma Scale*

GOS - *Glasgow Outcome Score*

ICP - *Intra-Cranial pressure*

MRI - *Magnetic Resonance Imaging*

MVA - *Motor Vehicle Accident*

NPV - *Negative Predictive Value*

ONSD - *Optic Nerve Sheath Diameter*

OR - *Odds Ratio*

PPV - *Positive Predictive Value*

PVA - *Pedestrian Vehicle Accident*

TBI - *Traumatic Brain Injury*

CHAPTER 1

1.1 INTRODUCTION

Traumatic brain injury (TBI) is very common in our setting and puts a strain on the healthcare system and social welfare services. There are no formal statistics reported locally, however we treat many patients with TBI due to assaults, motor vehicle accidents (MVA) and falls at the two major hospitals in Johannesburg. The estimated annual incidence of TBI in Europe is about 235 per 100,000, with mortality rate of 15.4 per 100,000 mainly due to motor vehicle accidents and falls.[1] In recent surveys the mortality rates in the United Sates were estimated at 18.4 per 100,000.[1]

TBI is a common cause of major disability and loss of income among young and middle aged South Africans in the cities. The development of reliable prognostic factors in addition to the existing ones would help guide therapy and allow prioritization of resources for patients with severe TBI.

Raised intracranial pressure (ICP) is a significant modifiable/treatable factor that directly impacts on outcome in patients with severe TBI.[1-7] Currently ICP can be reliably measured using invasive methods/micro catheter such as intra-ventricular, intra-parenchymal and subdural catheters.[2, 3] These invasive methods are not always available/feasible and are associated with risks and complications such as intra-cranial bleeds, device malfunctioning, zero drift and sepsis.[2, 3]

Indications for ICP monitoring in TBI [2, 3, 8]

- GCS<9 and an abnormal CT brain (CTB)
- GCS <9 and normal scan plus any two of the following:
  Hypotension (Systolic BP < 90mmHg)

  Abnormal posturing (decerebrating/decorticating)

  Age: >40years

Other indications include:

- Malignant infarction
- CNS Infections
- Hepatic encephalopathy
- Hypoxic brain injury

Numerous studies have demonstrated the direct correlation of ICP and Optic Nerve Sheath Diameter (ONSD) as measured noninvasively on Magnetic Resonance Imaging (MRI) brain, Computed Tomography (CT) scan brain as well as Trans-orbital Ultrasound with varying specificities and sensitivities depending on the population, imaging modality and ONSD cut off measurements used.[1-7, 9-10]

The optic nerve is an extension of the central nervous system (CNS), covered by the arachnoid and dura matter containing cerebrospinal fluid (CSF). During raised ICP the CSF around the optic nerve increases, causing an increase in the ONSD. The ONSD distension is maximal 3mm behind the eyeball and can be measured noninvasively by radiological modalities mentioned above.[1-7, 9-11] There is no consensus regarding the normal ONSD, it varies in children, adults and among different populations.[10, 11]

The Rotterdam score is another verified/investigated method used to detect raised ICP. It's a scoring system, based on CT brain features, comprised of the state of Basal cisterns, Midline shift, Epidural mass lesion, Traumatic Subarachnoid haemorrhage and/or intra-ventricular blood (Appendix D). The Rotterdam score predicted six months mortality as follows, Score 1 = 0%; Score 2 = 7%; Score 3 = 16%; Score 4 = 26%; Score 5 = 53% and score 6 = 61%.[12]

Hypothesis:

Increased Optic Nerve Sheath Diameter is associated with raised intracranial pressure and worse neurological outcome.

1.2 LITERATURE REVIEW

Legrand et al. demonstrated a strong independent relationship between the ONSD on the initial CTB and mortality rate among severe TBI in a prospective study of 77 patients.[1] The mean ONSD on initial CTB was 7.8 +/- 0.1mm in non-survivors compared to 6.8 +/- 0.1mm in survivors (P = 0.001). He concluded that the ONSD on CTB is independently associated with mortality rate in severe TBI when =/> 7.3mm cut off is used (Sensitivity = 86.4% and Specificity = 74.6%).[1] However, his study had a small sample and an element of potential bias. Only seven of his 77 patients had an invasive ICP monitor.

Review article by Raboel et al. concluded that invasive monitoring of ICP is currently the only option for reliable ICP measurement and that non-invasive methods fail to measure ICP reliably to be used as a routine alternative to invasive methods.[3]

A retrospective cohort of 220 patients by Sekhon et al. conducted between April 2006 and May 2012 concluded that ONSD measured on CTB was independently associated with ICP and mortality.[4] It was also reported that each 1mm increase in ONSD was associated with a two-fold increase in hospital mortality (OR 2.0, 95% CI and P = 0.007).[4] Another retrospective cohort between 2009 and 2013, with 57 patients reported a strong correlation between ICP and ONSD (P<0.001)[9]. With an ONSD cut off of 6.0mm, the sensitivity was 97%, specificity 42% as well as PPV of 67% and NPV of 92%.[9]

Masquere et al. argued that the results by Legrand et al. needs further confirmation of the reliability of the ONSD measurements after realignment of the optic nerve plane and measurements in several axis, owing to the sinuous course of the optic nerve in the orbit and the presence of the intra-orbital fat.[6]

In a retrospective analysis of the MRI (T2 sequence) of 38 patients who required an invasive ICP monitoring (intra-parenchymal catheter) after severe TBI and 36 healthy volunteers, an enlarged ONSD was a predictor of raised ICP with best cut off value of 5.82mm (PPV = 92% and NPV 100% when ONSD was < 5.30mm) leading the authors to conclude that ONSD on MRI can provide the prediction of the likelihood of significant ICP.[11] Again, the small sample size and the fact that MRI scans are not

routinely used in TBI patients owing to long acquisition times and limited availability among other factors add to the limitations of this study.

To prevent brain damage or death, the diagnosis of elevated intracranial pressure should be prompt. Raised ICP is transmitted to the subarachoid space surrounding the optic nerve, causing the nerve sheath to expand and has been correlated with clinical symptoms or CT abnormalities in numerous studies.[13] Kimberly et al demonstrated the correlation of raised ICP (>20cmH_20) and ONSD >5mm (on ultrasound) with 88% sensitivity and 93% specificity in the prospective, blinded, observational study of 15 adult patients.

There is a possibility that the ONSD may correlate with eyeball size, form and/or optic canal which might in turn influence the current methods of ONSD measurement.[14] Vaiman *et al* concluded that the Optic nerve sheath diameter/Eyeball Transverse diameter (ONSD/ETD) index on CT scan is more precise than the ONSD measurement itself and that, ONSD measurements 10mm from the globe gives the most stable results.

Kim et al concluded that ONSD may be used as a screening tool for detection of raised ICP and to evaluate ICP sequentially during mechanical ventilation after demonstrating the dynamic changes in ICP associated with $ETCO_2$.[15]

In a study of 519 healthy Chinese adults, Chen et al found the median ONSD 3mm behind the globe to be 5.1mm and the 95th percentile of 5.9mm on ultrasound. The ONSD is correlated with OND, while independent of gender, age, height, weight and ETD.[16]

Among 400 Nigerian adult participants, Ismail found no significant correlation of ONSD with side (left vs right), age and/or sex, thus allowing uniform reference values for adults.[17]

1.3 Justification of the Study

The development of reliable prognostic parameters in addition to the existing ones would help guide therapy and allow prioritization of resources for patients with severe TBI.

The ONSD varies in children, adults and different populations therefore, the establishment of an average ONSD in our adult population will set the groundwork for future research studies.

A high volume of TBI patients in our setting provides us with an opportunity to improve on patient care in order to optimize clinical outcomes.

1.4 Study Aim and Objective

1. Determine an average ONSD among adult patients with normal CTB presenting at CHBAH and CMJAH.
2. To examine the relationship between the ONSD on CTB and outcome upon discharge or thirty days (whichever comes first) in patients presenting with severe traumatic brain injury using the Glasgow Outcome Scale score in our setting.

CHAPTER 2: METHODS

2.1 Research design.

A prospective observational study was done at the two academic hospitals in Johannesburg (Chris Hani Baragwanath Academic Hospital and Charlotte Maxeke Johannesburg Academic Hospital).

2.2 Setting and Period of Study

This study was conducted at Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) over a period of 6 months from July to December 2015.

2.3 Patient Selection

2.3.1 Inclusion Criteria

- Severe traumatic brain injury (GCS<9).
- >18yrs of age.
- CTB done within 48hrs of TBI.

2.3.2 Exclusion Criteria

- Patients with multiple injuries.
- Penetrating head injury.
- Direct orbital/Eye trauma.
- Pre-existing ocular disease e.g. Glaucoma, optic atrophy etc.
- Previous/existing neurological conditions e.g. Brain tumour, hydrocephalus, cerebral aneurysm etc.

<u>Control group</u>

Adult patients (>18yrs) presenting with concussion as well as other patients who had normal brain scans between July and December 2015.

2.3.3 Limitations

Small sample size due to time constraints.

Lack of invasive ICP monitoring in the majority of patients will affect the assessment of the direct link between ONSD and ICP.

2.3.4 Measurements

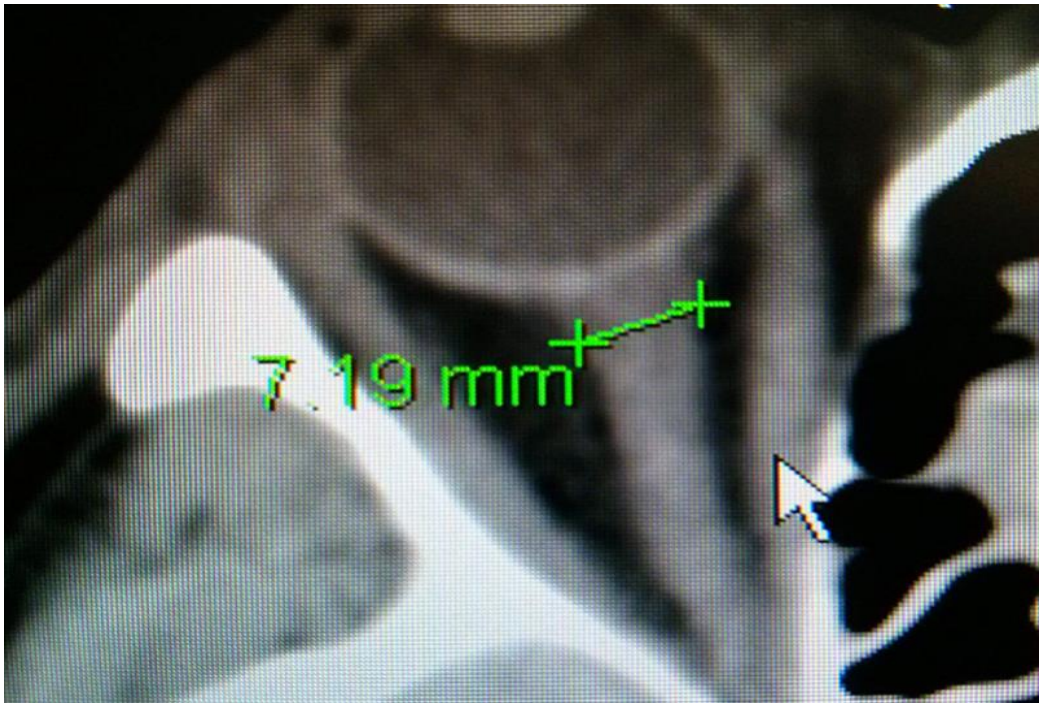


Figure 2.3.4.1: Optic Nerve Sheath Diameter measurement on CT scan

The ONSD will be measured by a radiologist not directly involved in patient care on an admission CTB on each side using the following technique (Figure 2.3.4.1):

- Using the axial CTB on abdominal/chest window.
- Diameter (ONSD) measured 3mm behind the eyeball, 90deg to the long axis of the optic nerve on the level of maximum dilatation.
- Using electronic callipers to measure the ONSD.
- All scans will be done in a standardized manner (horizontal plane, with head immobilized and gantry at Zero degrees).

2.3.5 Data analysis

A total of 53 patients met the inclusion criteria for the study, 13 patients were excluded as their scans couldn’t be retrieved. The data was captured on an Excel spreadsheet and analysed using means, graphs and tables. Chi test was performed to assess the statistical significance, the p value of < 0.05 would be considered statistically significant.

CHAPTER 3

3.1 Results

The study was conducted at two academic hospitals, Chris Hani Baragwanath Academic Hospital and Charlotte Maxeke Johannesburg Academic Hospital with 11 and 8 ICU beds respectively.

Of the 53 patients who met the inclusion criteria, 13 patients were disqualified due to unavailability of the CT scans. A total of 40 consecutive patients with severe traumatic brain injury were enrolled in the study from July to December 2015, 31 patients from CHBAH and 9 patients were from CMJAH. In addition a total of 42 adult patients who had normal scans during the study period were enrolled in the study, their ONSD were measured on CTB and analysed to establish an average ONSD in normal adults.

In total, 82 pairs of ONSD were assessed in 82 study candidates (40 TBI patients and 42 controls).

Collected data for TBI participants includes, age, gender, mechanism of injury, GCS, Rotterdam score, Optic Nerve Sheath Diameter, ICU length of stay and the GOS on discharge or thirty days. The in-hospital mortality and neurological outcome on discharge were analysed in 40 patients with severe traumatic brain injury.

Demographics

Only four of forty patients were between the ages of 51-65yrs (10%) and one patient (3%) over 65yrs of age. See figure 3.1 below.

The majority of patients with severe TBI in our study were young adult males(n=37) versus (3%) females.

Figure 3.2 below illustrates gender of participants.

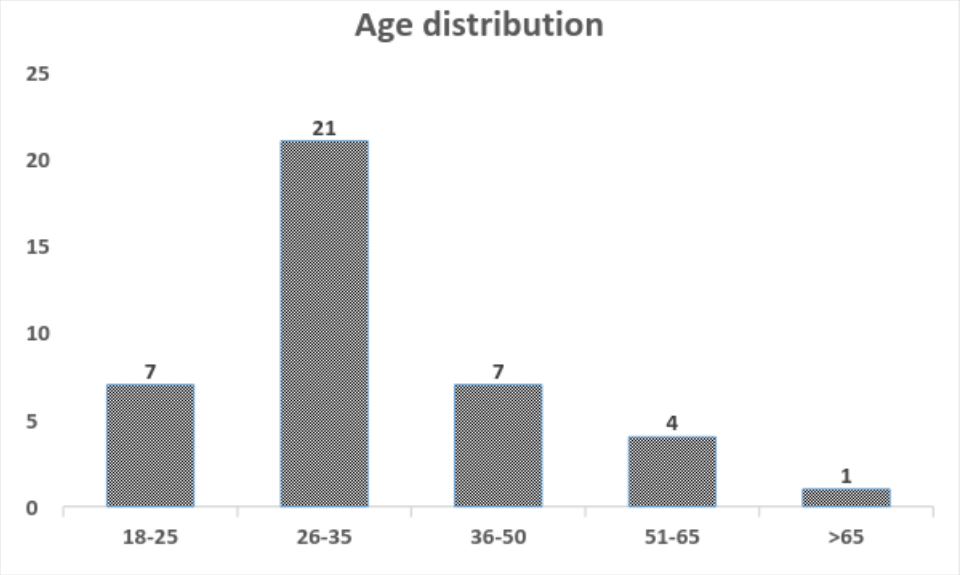


Figure 3.1: Age distribution

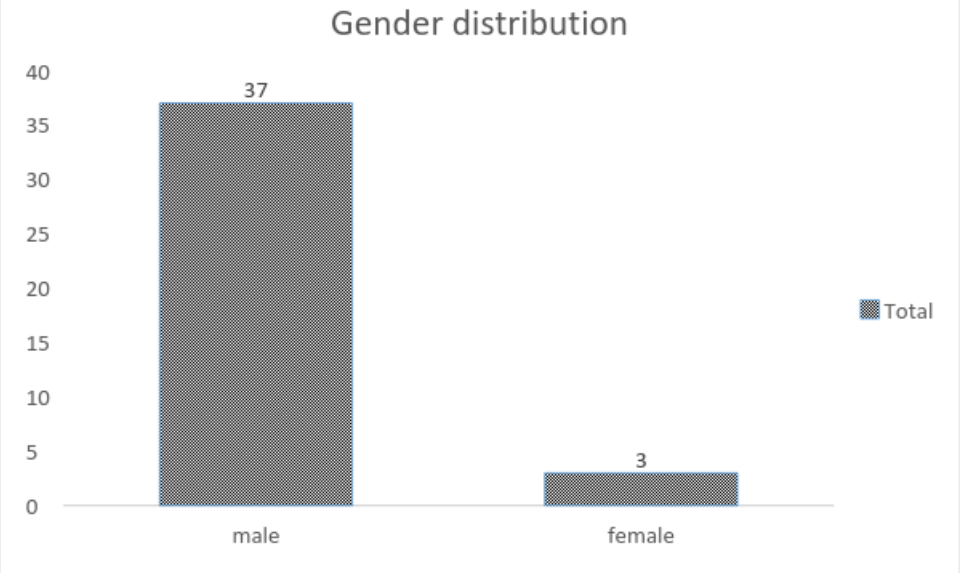


Figure 3.2: Gender

Mechanism of injury

Assaults and MVA/PVA accounted for most of these injuries, 43% (n=17) and 28% (n=11) respectively as demonstrated in Figure 3.3 below. Other mechanisms of injury included a heterogeneous group of patients (n=12) who had clear evidence of trauma, but it was not possible to ascertain how they sustained TBI.

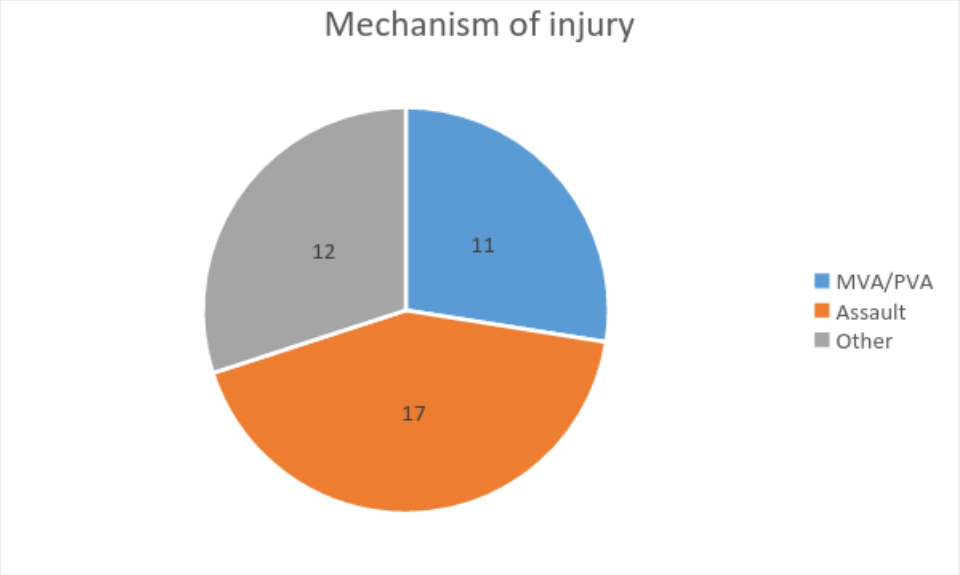


Figure 3.3: Mechanism of injury

Clinical Findings

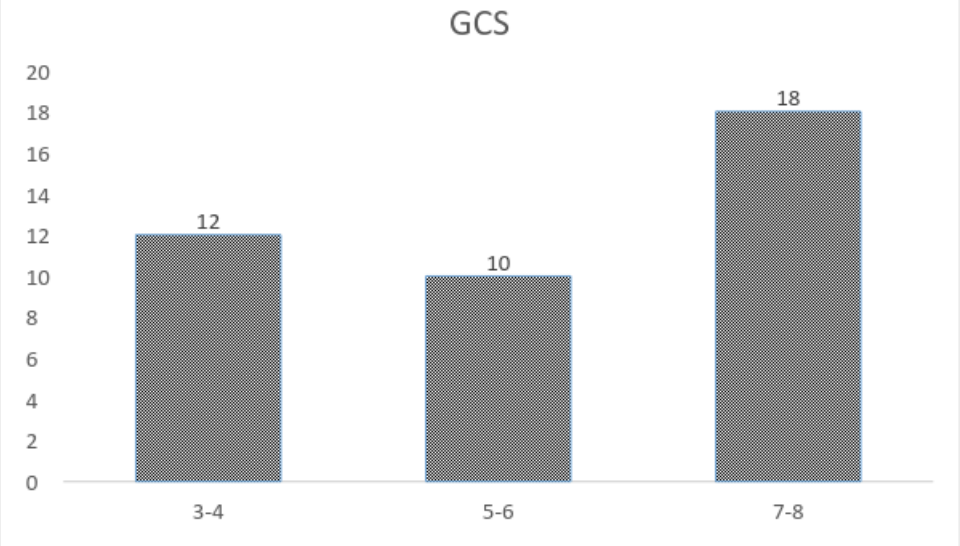


Figure 3.4: GCS

All patients had severe TBI with post resuscitation GCS <9. Patients GCS was assigned to one of the three categories, as shown in Figure 3.4 above. Category 1 (GCS 3-4) had 12 patients (30%), category 2 (GCS 5-6) had 10 patients (25%), and the majority of the patients (45%) were in category 3 (GSC 7-8).

Radiological findings

- Rotterdam Score

The Rotterdam score (Appendix D) is a radiological assessment tool used to evaluate the severity of TBI.

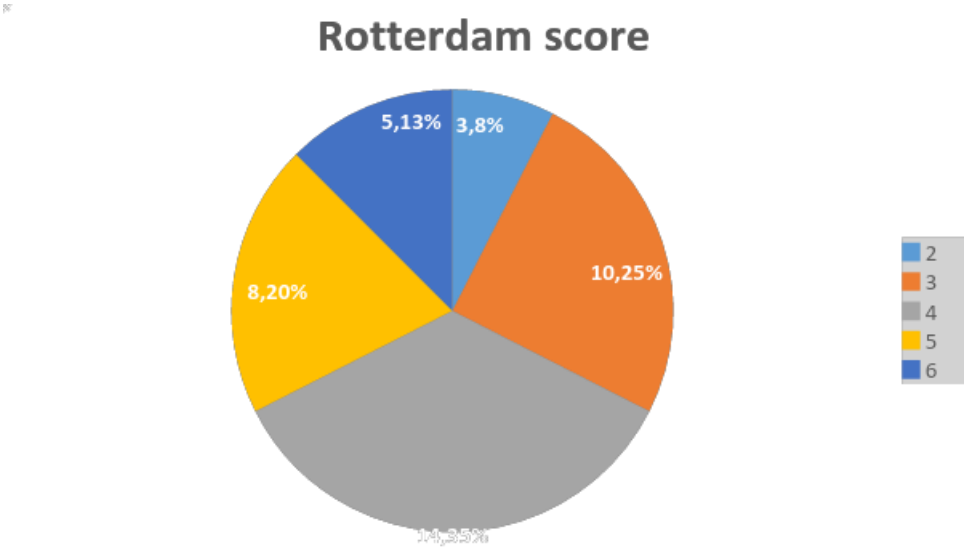


Figure 3.5: Rotterdam Score

The Rotterdam score was evaluated in all patients, 35% (n=14) of patients had a score of 4, followed by 25% (n=10) with a score of 3, 20% (n=8) with a score of 5, 13% (n=5) with a score of 6 and 7% (n=3) with a score of 2. See Figure 3.5

- Optic Nerve Sheath Diameter

The ONSD of normal scans is presented on the chart below.

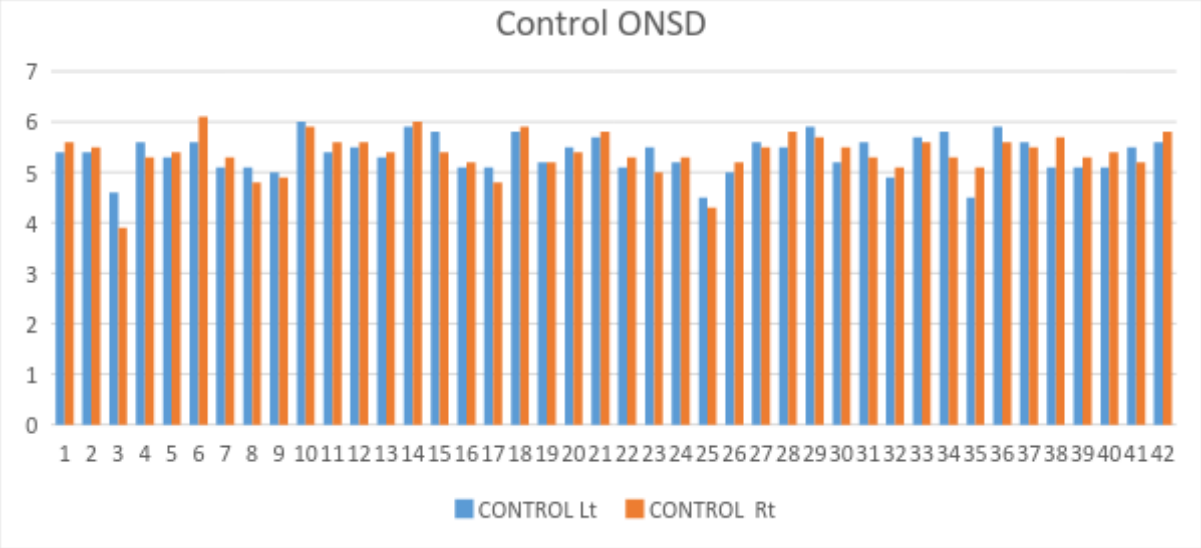


Figure 3.6: Control ONSD

The overall average ONSD in 42 (controls) participants with normal CTB is 5.36mm, with the right and left average ONSD of 5.37 and 5.36mm respectively, ranging from 3.9mm to 6.1mm.

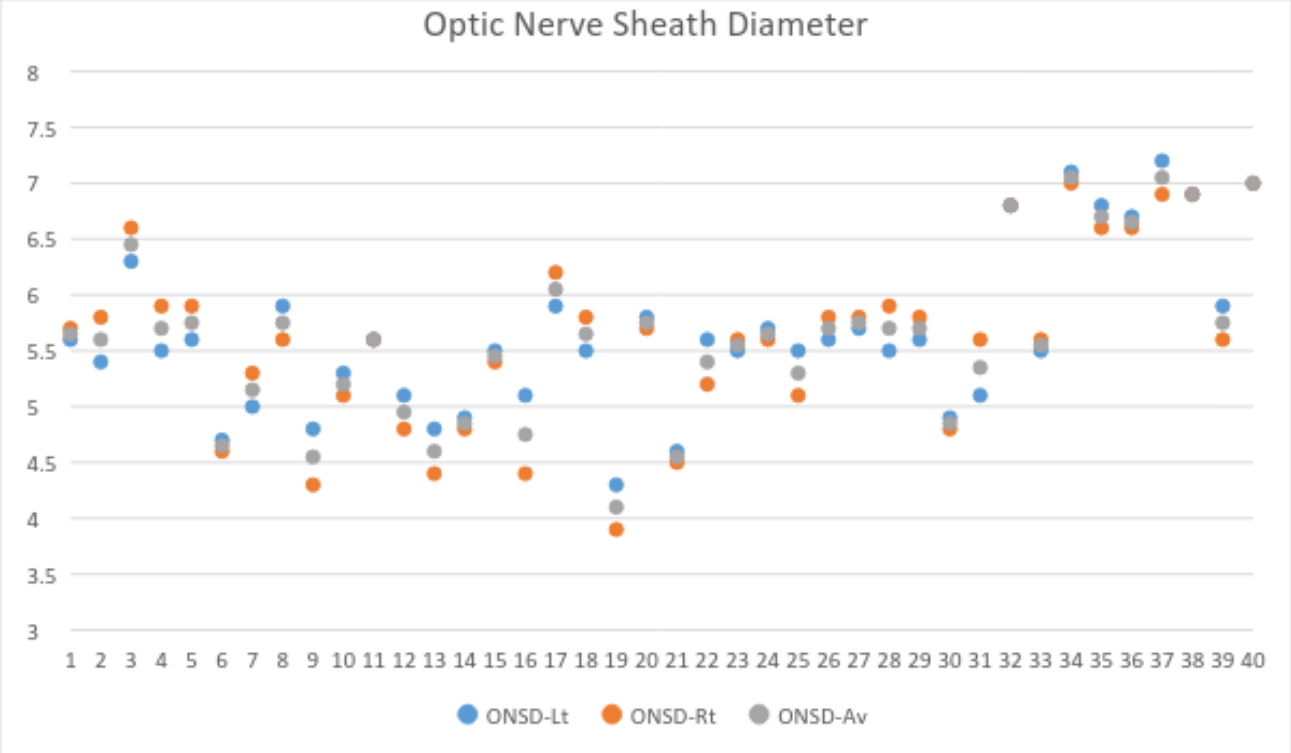


Figure 3.7: Optic Nerve Sheath Diameter in TBI participants

The average ONSD in 40 TBI patients ranged from 4.1mm to 7.05mm, with a mean of 5.6mm. Most patients with increased ONSD had category 1 and 2 GCS.

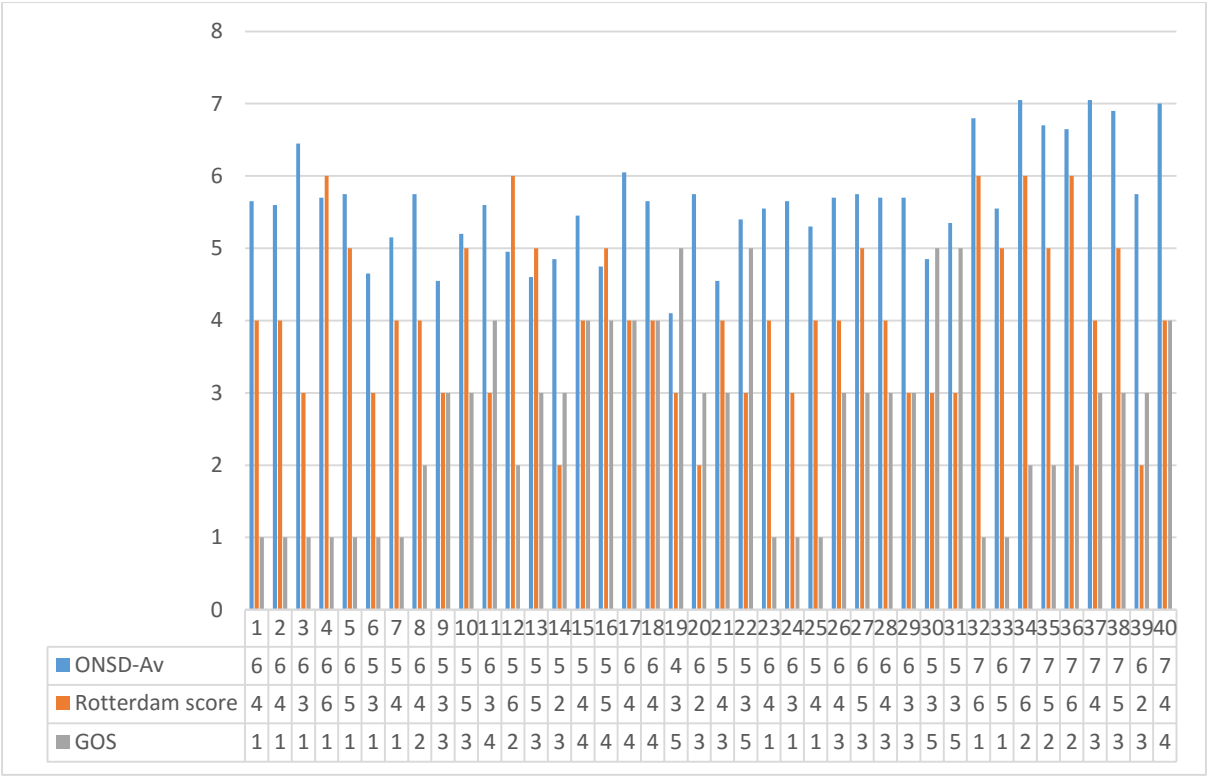


Figure 3.8 Average ONSD vs Rotterdam Score as a predictor of GOS

Out of 40 participants 30% died (GOS 1), 13% were in a vegetative state (GOS 2), 33% had severe disability (GOS 3), 15% had moderate disability (GOS 4) and 10% good recovery (GOS 5). Of the patients who died, the Rotterdam score ranged between 3 and 6 (Rotterdam score of 3, 3 participants; Rotterdam score of 4, 5 participants; Rotterdam score of 5 and 6 had 2 participants each), no patients with a Rotterdam score <3 died. The average ONSD in TBI patients was 5.63mm. For non-survivors the ONSD ranged from 4.65mm to 6.8mm, only three non survivors had an ONSD below 5.36, all other non survivors had ONSD > 5.5mm. Severe disability and vegetative states presented with ONSD of between 4.55 and 7.05mm. High mortality correlated with increased ONSD of 5.65mm and Rotterdam score of three and above.

ICP monitor

Only 5 out of 40 patients (13%) had an ICP monitor inserted, it ranged between 21 and 31mmHg. Increased ICP was associated with ONSD > 5.5mm. Most patient did not have ICP monitors due to limited resources and the discretion of the treating

doctor. Lack of invasive ICP monitoring in most participants prevents the direct evaluation of intracranial hypertension and ONSD.

ICU length of stay

Length of ICU stay ranged from two days to thirty days. Most patients with prolonged ICU length of stay had either severe disability or were in a vegetative state, their prolonged ICU stay was further compounded by other complications eg. Lower respiratory tract infections.

Glasgow Outcome Scale

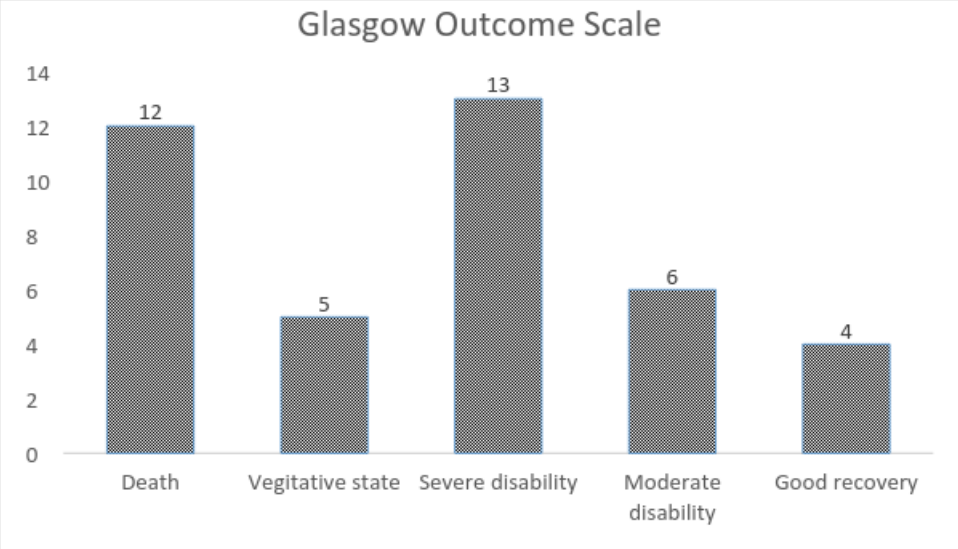


Figure 3.9: GOS

Out of 40 TBI participants, 30% died, 13% were in a vegetative state, 33% had severe disability, 15% had moderate disability and 10% had good recovery, as demonstrated in Figure 3.9.

The GOS was categorized into death (GOS 1), poor outcome (GOS 2 and 3) and good outcome (GOS 4 and 5) as presented on Table 3.1 below.

Non-survivors and poor outcome participants had ONSD >5.5mm, whereas good outcome participants had ONSD <5.5mm.

Table 3.1: ONSD vs Rotterdam score as predictors of outcome

VARIABLE	*DEATH*	*POOR OUTCOME*	*GOOD OUTCOME*
ONSD	5.65mm	5.73mm	5.43mm
ROTTERDAM	3 - 6	3 - 6	1 -2
ICU LOS	2 – 7days	1 – 4 weeks	2 – 7 days

The table above show that good outcome patients had an average ONSD of 5.43mm vs 5.65mm in patients who died. The difference between death and poor outcome groups could be explained by the following reasons:

- The patients may have died as a result of the primary severe head injury.
- The use of hyperosmolar therapy prior to CTB in some poor surgical candidates presenting in resus room may affect the ONSD.
- The duration between the primary injury and time of CTB may be short, and unable to demonstrate the secondary effect (ONSD distension) of raised ICP.

Data analysis

An arbitrary ONSD cut off value of 5.5mm was used. The ONSD cut off value was based on the literature review, average ONSD in adults with normal CTB and the average ONSD in TBI patients with Good outcome.

Table 3.2: ONSD as a predictor of outcome

	DEATH	GOOD OUTCOME	TOTAL
ONSD >5.5mm	9	4	13
ONSD <5.5mm	3	6	9
	12	10	22

The sensitivity of the ONSD as a predictor of death (GOS1) was 75% with a Specificity of 60% when using ONSD >5.5mm with a p-value of 0.096 which is not statistically significant.

Table 3.3 Correlation of ONSD and Rotterdam score

	Rotterdam <3	Rotterdam >3	Total
ONSD >5.5mm	2	23	25
ONSD <5.5mm	1	14	15
TOTAL	3	37	40

The correlation of ONSD and Rotterdam score had a p-value of 0.876824, proving that the results are not statistically significant.

CHAPTER 4

4.1 DISCUSSION

To date numerous studies to evaluate the relationship between the ONSD and raised ICP have been performed, mostly using the trans-orbital ultrasound technique. The reported normal ONSD varies in children, adults and different populations.

The direct link demonstrated in previous studies between ICP and clinical outcomes forms the basis of this research.

Although our results demonstrated a relationship between ONSD and GOS as shown in table 3.2, the findings were not statistically significant and our hypothesis could not be accepted. Our findings are not in keeping with most international studies performed to date. Reasons for the discrepancy may be due to a number of reasons such as, the effect of primary TBI on outcomes, where severe primary injury kills before ONSD increases, the effect of time between TBI and scan, where short time has implications for ONSD increases as well as the effects of other secondary insults, eg. Hypoxia, hypercarbia etc.

Study by Raboel et al. also concluded that non-invasive methods failed to measure ICP reliably to be used as routine alternatives to invasive ICP monitoring.

The correlation between the ONSD and Rotterdam score was also not statistically significant, making the ONSD an unreliable marker for prognostication in severe TBI patients.

Our current methods of ONSD measurements may be flawed due to a number of anatomic variations as suggested by Masquere et al., and may need to be revised in order to be population specific and sensitive.

CHAPTER 5

5.1 CONCLUSION

Our results show that the ONSD has some value in grading the severity of TBI. When ONSD is increased it correlates with poor outcomes and therefore may be used to assess the risk of raised ICP and to strengthen the indications for invasive ICP monitoring. The results are not statistically significant suggesting that the ONSD may not be sensitive nor specific for predicting outcome when used alone. It may however, not be used as a sole surrogate marker of increased ICP.

Further multicentre studies using invasive ICP monitoring needs to be performed to evaluate the relationship between ONSD, ICP and Outcome.

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