Outcome analysis and outcome predictors of severe traumatic brain injury in patients admitted to a level 1 trauma unit.

A dissertation submitted in the fulfilment of the requirements for the degree of Master of Health Sciences in Emergency Medical Care in the Faculty of Health Sciences at the Durban University of Technology

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PREFACE AND DECLARATION

This study was conducted at Inkosi Albert Luthuli Central Hospital located in the eThekwini district, under the supervision of Dr Simpiwe Sobuwa and Prof. Timothy Hardcastle.

This is to certify that this work is entirely my own and not that of any other person, unless explicitly acknowledged (including citation of published and unpublished sources). The work has not previously been submitted in any form to the University of Technology or to any other institution for assessment or for any other purpose.

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Signed:

Date: 01/11/2022

ETHICAL CLEARANCE

This is to certify that the research studies conducted for the purpose of this study dissertation have the approval of the Biomedical Research Ethics Committee (BREC) of the University of Kwa-Zulu Natal (UKZN) in KwaZulu-Natal.

Biomedical Research Ethics Committee REF: BCA207/09

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ABSTRACT

Introduction: Rapid transportation to the relevant trauma facility is crucial in the mortality and morbidity of severely injured patients. Traumatic brain injury (TBI) remains the source of international mortality and morbidity, surpassing all other trauma-related injuries. Predicting patient outcomes in TBIs involves formulating a logical association between the patient's initial assessment and overall patient outcome.

Objective: The purpose of this study was to analyse patient outcome in severe TBI according to their transportation methods to a level 1 trauma facility and the associated outcome predictors.

Methods: This study was a retrospective, quantitative study based on patient outcomes and the associated outcome predictors in patients transported to Inkosi Albert Luthuli Central Hospital (IALCH) by different transport methods between January 2017 to December 2018. All patients were categorised according to age and the severity of traumatic brain injury. All patients older than 12 years of age were included in this study. Patients classified as having a severe traumatic brain injury (TBI) based on the Glasgow Coma Score (GCS) and/or CT scan findings were included in this study.

Results: There were 202 patients included in the study; 167 were males. Motor vehicle collision was the most common mechanism of injury, accounting for 41.1% of patients' injuries in the study. Mortality was significantly greater in direct admissions compared to interhospital transfers ($p<0.001$). Patients who were directly admitted to IALCH were admitted for a shorter length of stay compared to inter-hospital transfer. A significantly higher mortality rate in hypotensive patients on arrival at the emergency department (ED) was identified ($p=0.02$). This study revealed a borderline significance between hyperglycemia and mortality, suggesting that further research would be interesting ($p=0.07$). New injury severity score (NISS), revised trauma score (RTS) and Glasgow Coma Scale (GCS) demonstrated good predictions of mortality. However, the results of this study suggest that the new injury severity score was the most accurate predictor of outcome.

Conclusion: These results suggest that assessments of physiological/anatomical scoring systems and predictors of the outcome can be a valuable component in

predicting mortality in cases of severe traumatic brain injury and that the mechanism of the injury influences mortality and the length of stay.

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LIST OF ABBREVIATIONS

AIS: Abbreviated injury scale

ALS: Advanced life support

BLS: Basic life support

CBF: Cerebral blood flow

CPP: Cerebral perfusion pressure

CSF: Cerebral spinal fluid

CSI: Cervical spine injury

CT: Computed tomography

DA: Direct admission

DAI: Diffuse axonal injury

ED: Emergency department

EDH: Epidural haemorrhage

EMS: Emergency medical service

EtCO2: End-tidal carbon dioxide

EVD: External ventricular drain

GCS: Glasgow coma scale

GOS: Glasgow outcome scale

GOSE: Glasgow outcome scale extended

GSW: Gunshot wound

HGT: Hemoglucose test

HPCSA: Health Professionals Council of South Africa

IALCH: Inkosi Albert Luthuli Central Hospital

ICD: International Classification of Diseases

ICP: Intracranial pressure

IHT: Interhospital transfers

ILS: Intermediate life support

IMPACT: International Mission on Prognosis and Analysis of Clinical trials

IPH: Intraparenchymal haemorrhage

ISS: Injury severity score

LOS: Length of stay

MAP: Mean arterial pressure

MOI: Mechanism of injury

MRI: Magnetic resonance imaging

MVC: Motor vehicle collision

NIH: National institute of health

NISS: New injury severity score

pO2: Partial pressure of oxygen

RR: Respiratory rate

RTS: Revised trauma score

SA: South Africa

SAH: Subarachnoid haemorrhage

SATS: South African Triage Scale

SBP: Systolic blood pressure

SDH: Subdural haemorrhage

TBI: Traumatic brain injury

TXA: Tranexamic acid

VAP: Ventilator-associated pneumonia

LIST OF TERMS

Traumatic brain injury (TBI): Occurs from an insult to the brain from an external mechanical force that may lead to permanent or temporary changes in cognitive, physical and psychological functions with changes in the level of consciousness (Malale *et al*., 2020).

Mortality: Mortality is associated with the number of deaths caused by the incidence of a health event (Hernandez and Kim, 2022).

Morbidity: The state of presenting symptoms from the relative incidence of a particular disease or condition (Hernandez and Kim, 2022).

Outcome predictors: For the purposes of this study, outcome predictors refer to factors that affect mortality.

Chapter 1: Introduction

Background

Traumatic brain injury (TBI) is the primary cause of mortality in critical trauma patients, accounting for approximately 30% of traumatic deaths (Jochems *et al*., 2018). Mortality rates vastly differ amongst level 1 trauma facilities internationally (Jochems *et al*., 2018). TBI is caused by an external force on the head that results in anatomical injury and functional disability of the brain and other components of the head, such as the meninges, scalp and skull (Silva *et al*., 2018). TBI consists of primary and secondary TBI. Primary TBI is caused by the initial external physical force and may progress to secondary TBI. Increased intracranial pressure (ICP), hypotension, hypoxia, anaemia, seizures, hypoglycaemia and hyperthermia contribute to secondary brain injury (Okidi *et al*., 2020). Prevention of secondary injury in TBI and rapid, appropriate patient management is crucial to improve patient outcome (Okidi *et al*., 2020). Often, TBI may result in severe functional impairment, such as unresponsive wakefulness syndrome, where the patient is alive yet remains unconscious. In such instances, and when medical treatment is ineffective, withdrawal of life-sustaining treatment can be initiated (Jochems *et al*., 2018).

Determining a reliable prediction of mortality is difficult, particularly in the pre-hospital environment. The most influential independent components to predict mortality are age, Glasgow Coma Scale (GCS) – motor score, Marshall CT classification and traumatic subarachnoid haemorrhage (Silva *et al*., 2018). Other major variables include hypotension, hypoxia, specific CT scan characteristics, glucose, coagulopathy and haemoglobin (Silva *et al*., 2018). Classifications of TBI differ; however, GCS appears to be the most frequently utilised tool to classify TBI severity (Okidi *et al*., 2020). GCS scores are categorised as mild (13-15), moderate (9-12) and severe (3-8).

Research problem

Although there are limited studies concerning the prevalence of TBI in South Africa, an incidence of 316 cases per 100 000 per year has been reported (Maasdorp *et al*., 2020). The majority of patients who sustain TBI in South Africa are young, healthy adults who survive but develop cognitive or functional disabilities (Maasdorp *et al*., 2020). SA is considered a resource-limited country and, therefore, has limited

discharge rehabilitation or long-term care facilities for patients with cognitive and/or functional disabilities in the provincial division (Maasdorp *et al*., 2020). Effective patient management is best reflected by mortality in patients transported directly to a level 1 trauma facility. Direct transportation reduces any delay in definitive patient management and improves patient outcome (Cheddie *et al*., 2011).

The “Golden Hour” suggests a decrease in mortality and morbidity if definitive treatment is activated within the first hour after injury (Vanderschuren and Mckune, 2015). Chowdhury *et al*. 2009, suggest an improved patient outcome in patients transported to an appointed trauma facility within the “Golden Hour” (Chowdhury *et al*., 2016). Reduced pre-hospital on-scene time was also associated with improved outcome in trauma patients that sustained critical head injuries, thoracic injuries and intra-abdominal haemorrhage (Chowdhury *et al*., 2016). Regardless of varying evidence about response time and the “Golden Hour”, it is logical to presume that rapid transportation to a facility for definitive care will reduce complications and improve patient outcome (Chowdhury *et al*., 2016). This study revealed that majority of patients were transported to the closest facility directly from the scene and had a better outcome compared to those transported directly to a level 1 facility.

There is limited literature available on outcome predictors and outcome analysis of severe TBI in patients admitted to a level 1 trauma facility in South Africa (SA), as most studies are performed outside the South African context. TBI remains a high burden on injury and mortality in SA (Jerome *et al*., 2017). Predicting outcomes in severe TBI remains an under-researched topic, highlighting the need for reliable studies within the South African context.

Researcher’s interest in the study

The researcher qualified as an emergency care practitioner in 2019, during which she treated several patients with traumatic brain injury both in the pre-hospital environment and in the emergency department of provincial hospitals. During her experience as an operational paramedic, she observed the high prevalence of traumatic brain injury in the pre-hospital environment and the associated mortality. This sparked an interest in predicting patient outcome and effective management to improve patient outcome. As a pre-hospital healthcare worker, decision-making regarding transportation to specific facilities that can provide definitive care is burdensome. It was observed that the

majority of trauma-related injury patients were not transported to a level 1 trauma unit in the Ethekwini metropole but rather to the closest hospital delaying definitive patient management and resulting in poor patient outcome.

Aims and objectives

1.4.1 Aim of the study

The aim of this study was to describe and predict outcomes in severe traumatic brain injury in patients admitted to a level 1 trauma facility in order to make evidence-based recommendations and contribute to reliable literature regarding traumatic brain injury in the South African context.

1.4.2 Objectives of the study

- Describe patient outcome following severe traumatic brain injury according to their transport method to a level 1 facility.
- Determine the relationship between the transport method to the hospital and outcomes following severe traumatic brain injury.
- Describe outcome predictors that predict mortality in severe traumatic brain injury.

Structure of the dissertation

Chapter 1: Introduction

Chapter one of this study introduced the research topic by contributing knowledge on the reported and global burden of severe traumatic brain injury. Thereafter, the chapter focused on discussing predictors of mortality of severe TBI. The chapter concluded by presenting the aim and objectives of the study, together with the research problem and the researcher's interest in the study.

Chapter 2: Literature review

Chapter 2 extensively reviews literature related to traumatic brain injury. The chapter introduces the topic by discussing the prevalence of TBI world-wide. The chapter then explores the pathophysiology of TBI; outcome predictors, including anatomical and physiological scoring systems, as well as clinical predictors such as demographics, GCS, hypotension, and pupil response; CT scan findings and finally, management. The chapter concludes by outlining pre-hospital triage of patients to assist with identifying critically injured patients.

Chapter 3: Research design and methodology

Chapter three reviews the research process undertaken to conduct this study. This chapter begins by introducing the research design used in the study. Thereafter, the chapter describes the study setting, quantitative phase, study population and sampling techniques used to conduct this study. The chapter goes on to describe the inclusion criteria, exclusion criteria, data collection methods, and data analysis. Finally, the chapter explores the validity and reliability of the study as well as the ethical considerations observed during the study.

Chapter 4: Results

The results of the study were presented as figures and tables. The chapter starts by describing the demographics, method of transportation and mechanism of injury. The chapter thereafter proceeds to describe the length of stay, vital signs such as hypotension, hypoxia and hyperglycemia, and the physiological scoring systems. The chapter concludes by presenting patient complications during hospital admission.

Chapter 5: Discussion

In chapter five, the outcome and findings of the study are discussed and compared to the current existing literature regarding the topic. The discussion focuses on exploring mortality associated with different factors and outcome predictors. The chapter concludes by summarising the most significant findings of the results.

Chapter 6: Conclusion and recommendations

Chapter six concludes the research findings and provides guidance for predicting patient outcome in severe traumatic brain injury. Finally, the chapter suggests recommendations for future research and discusses the limitations of the study.

Conclusion

In this chapter, the background and introduction to severe TBI are discussed. Thereafter, the research problem, research aim, research objectives and structure of the dissertation are discussed. Lastly, this chapter presents the researcher's interest in the study topic and concludes the chapter. Chapter 2 extensively reviews the literature relating to severe TBI, outcome and outcome predictors.

Chapter 2

Literature Review

2.1 Introduction

This chapter seeks to review published literature relating to traumatic brain injury extensively. Firstly, the search strategy utilised by the researcher to identify literature pertinent to traumatic brain injury is discussed. Furthermore, the researcher accumulates and analyses historic literature on traumatic brain injury and the associated patient outcome, outcome predictors, management, and transportation methods to the hospital.

2.2 Search strategy

A search strategy refers to a composition of key terms used to search a database for relevant literature. These databases include numerous search engines, including Google, Google Scholar, PubMed, Science Direct, NCBI, SciELO and Medline. The literature used to construct this literature review largely includes journal articles, government documents and dissertations. Table 1 presents the keywords used to search the abovementioned databases.

Table 1: Key search words

Severe Traumatic Brain Injury
Outcome predictors in traumatic brain injury
EMS transportation methods of traumatic brain injury patients
Patient outcome in severe traumatic brain injury
Patient management in severe traumatic brain injury patients
Traumatic brain injury in South Africa

2.3 Epidemiology of traumatic brain injury

South African audits on trauma-related injuries indicate a high burden of injury due to interpersonal violence (Jerome *et al*., 2017). A study performed by Jerome and colleagues suggests a significant burden of traumatic brain injury, especially severe TBI (Jerome *et al*., 2017). An estimated 90% of international deaths due to injuries occur in low-and-middle-income countries (Norman *et al*., 2007). Of these, TBI accounts for universal mortality and morbidity more than any other trauma-related injury (Dewan *et al*., 2018). TBI affects approximately 10 million individuals yearly and

predominantly occurs in low and middle-income countries with inadequate health networks to address associated health outcomes (Hyder *et al*., 2007).

South Africa's burden of injuries comprises largely of violence and road traffic incidents (Norman *et al*., 2007). In South Africa, motor vehicle collisions and interpersonal violence are the principal causes of TBI (Kong *et al*., 2017). Transport-related injuries are more common in young males influenced by alcohol and drugs, increasing the burden on developing communities (Hardcastle *et al*., 2016). South Africa remains a low-to-middle-income country with a high burden of diseases. Although infectious and other diseases remain a crucial point in the burden of diseases, the trauma continues to be a major cause of mortality and morbidity, especially in individuals below forty years of age (Lutge *et al*., 2016). A large amount of resources have been dedicated to surveilling infections and other diseases, neglecting the magnitude of the trauma burden of disease (Norman *et al*., 2007). There has been a noticeable decrease in the incidence of traumatic brain injury in high-income countries as a result of public health rules such as the use of a helmet, seatbelt and health and safety regulations at the workplace (Khellaf *et al*., 2019). Approximately 60% of traumatic brain injury cases result in serious physical, psychological and social deficits, and a mortality rate of 30%-40% (Khellaf *et al*., 2019).

2.4 Traumatic brain injury

Traumatic brain injury is known as the silent epidemic because the majority of individuals living with the consequences of traumatic brain injury are not outspoken regarding the effects, and there is inadequate understanding regarding the injury (Peeters *et al*., 2015).

Traumatic brain injury is caused by an external mechanical force resulting in rapid movement of the brain inside the skull, causing injury to the brain (Prins *et al*., 2013). External mechanical force includes direct impact or penetration resulting in temporary disability, permanent disability, or social maladjustment (Anzai and Minoshima, 2011). The incident may be categorised as impact or non-impact depending if the head physically makes contact with an object (impact) or the individual experiences a rapid acceleration and deceleration motion (non-impact) (Prins *et al*., 2013). Injury to the brain results from angular – rotational forces, translational – linear forces or blunt force generating intracranial pressure gradients that produce shearing and strain forces.

These forces result in stretching and damage the axons, known as axonal injury or diffuse axonal injury (DAI) (Blennow *et al*., 2016).

Traumatic brain injury is separated into primary and secondary TBI. Primary TBI occurs during the initial impact of the head, resulting in the displacement of the brain within the skull (Prins *et al*., 2013). This may result from a direct contact force at the incident of injury. Diffuse axonal injury, epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, brain contusions and skull fractures are associated with primary TBI (Anzai and Minoshima, 2011). Traumatic brain injury constitutes a dynamic process involving primary parenchymal injury from initial impact followed by a systemic response. The effects of the systemic response include hypoxia, hypotension, cerebral oedema, and hypercarbia. Together, these will result in secondary brain injury (Rincon-Guio *et al*., 2017). Secondary brain injury involves a cascade of events that takes place over time as a consequence of progressing cellular events leading to further injury (Prins *et al*., 2013). This may occur within minutes or days after the initial traumatic impact (Anzai and Minoshima, 2011).

Severe TBI often includes cerebral oedema, herniation, and ischaemia (Anzai and Minoshima, 2011). Usually, the amount of blood flow to the brain remains consistent due to autoregulation (Anzai and Minoshima, 2011). If autoregulation fails, it results in an increase in mean arterial pressure, resulting in a decrease in cerebral perfusion pressure (Anzai and Minoshima, 2011).

Cerebral haematomas or cerebral contusions often result in a rise in intra-cranial or cerebral pressure. The brain becomes ischaemic when the cerebral perfusion pressure decreases < 50mmHg resulting in an increase in ICP, often leading to cerebral hypoxia, cerebral ischaemia, cerebral oedema, and brain herniation (Anzai and Minoshima, 2011). Anzai and Minoshima (2011) suggest that appropriate management and maintaining CPP and ICP is associated with improved patient outcome. Often, Glutamate and Aspartate are remarkably increased after traumatic brain injuries. Glutamate and Aspartate are excitatory neurotransmitters, which ultimately result in additional cell damage and cerebral oedema by causing the influx of chloride and sodium ions and mitochondrial dysfunction (Anzai and Minoshima, 2011). Excitatory neurotransmitters lead to an influx of calcium associated with cellular damage and the degrading of axonal conveyance (Anzai and Minoshima, 2011). Any

rise in extracellular potassium will lead to oedema, a rise in cytokine levels, ultimately contributing to inflammation and affecting secondary TBI. Another mechanism that affects secondary TBI involves a reduction in intracellular magnesium, which contributes to additional calcium inflow (Anzai and Minoshima, 2011).

TBI is categorised as mild, moderate, and severe TBI, which is based on the Glasgow Coma Scale (level of consciousness) measurement. Mild TBI is categorised as GCS 13-15, Moderate TBI 9-12 and severe TBI <9 (Prins *et al*., 2013). Mild to moderate TBI often manifests with symptoms such as headaches, amnesia, dizziness, and nausea that usually resolve within weeks of the injury (Prins *et al*., 2013). Although, individuals rarely develop long-term cognitive and behavioural complications (Prins *et al*., 2013). The Glasgow Coma Scale assesses the clinical state of the patients. Subsequently, it is essential to determine the type and severity of the injury by use of brain imaging. Cranial computed tomography (CT) is the suggested instrument for the initial assessment of traumatic brain injury in emergency services (Rincon-Guio *et al*., 2017).

The categorisation of severe TBI in accordance with either the Glasgow Coma Scale or the CT scan findings allows healthcare workers to determine an association between prognosis and surgical indications in a better-standardised system (Rincon-Guio *et al*., 2017).

Cerebral oedema

Even though numerous aspects contribute to increased mortality and morbidity related with TBI, cerebral oedema remains a crucial predictor of patient outcome (Donkin and Vink, 2010). Cerebral oedema and intracranial hypertension significantly increase mortality and morbidity post-TBI (Zusman *et al*., 2020). Cerebral oedema can be described as an expansion of the brain tissue water, including the brain cells and interstitial spaces (Jha *et al*., 2019). When the swelling includes the cells and the tissue parenchyma, ICP increases, resulting in compression of blood vessels, decreased blood flow to the tissues, and decreased oxygenation, which eventually causes herniation (Donkin and Vink, 2010). A vital correlation has been recognised between cerebral oedema, intracranial hypertension, and patient outcome in traumatic brain injury (Jha *et al*., 2019). These factors lead to brain herniation, permanent brain damage and death (Jha *et al*., 2019). Increased intracranial pressure may result from an increase in volume within the skull resulting from hematomas, contusions or

secondary brain injury processes (Jha *et al*., 2019). The development of the size of the hematoma is a major concern within the first few hours of post-injury. However, cerebral oedema is one of the leading causes of increased intracranial pressure (Jha *et al*., 2019). Any change in cerebral perfusion pressure and cerebral blood flow produces intracranial hypertension, which may progress to irreversible brain injury, herniation and death (Jha *et al*., 2019). Cerebral oedema often does not respond to medical therapy, making management challenging and resulting in irreversible injury with a mortality rate of up to 100% if left untreated (Abdelmalik *et al*., 2019). Surgical and medical interventions have been associated with a reduction in intracranial pressure and mortality (Abdelmalik *et al*., 2019).

Cerebral spinal fluid

Diagnosing cerebrospinal fluid (CSF) leakage remains challenging and raises the risk of acquiring infections of the central nervous system. A useful CSF examination involves placing a portion of the fluid on a white filter paper – CSF will create a halo surrounding the fluid. However, a mixture of blood with saline or tears will also produce a halo effect (Abdelmalik *et al*., 2019). Alternatively, the fluid is tested for beta-2 transferring at a laboratory (Abdelmalik *et al*., 2019).

Tension Pneumocephalus

Tension pneumocephalus occurs when the air is confined within the skull, unable to escape (Abdelmalik *et al*., 2019). This results in an increase in intracranial pressure, resulting in the compression of the brain (Abdelmalik *et al*., 2019). Management of tension pneumocephalus involves 100% oxygen therapy and flat bed rest but may require a decompressive burr-hole. It is believed that the oxygen exchanges with the nitrogen in the confined air and is then absorbed. However, there is insufficient information available to support the efficacy of the treatment (Abdelmalik *et al*., 2019).

2.5 Types of Traumatic Brain Injury

Traumatic brain injury can be divided into two categories:

Closed head injuries involve a blunt collision with the head, such as forceful injury to the head with a heavy object, while penetrating head injuries occur when the impact to the head results in skull fractures and contact with the brain parenchyma (Abdelmalik *et al*., 2019). A penetrating stab wound is usually caused by an object with a small surface area that impacts the cranium. It may form a slot skull fracture with

possible underlying tract hematoma (Muballe *et al*., 2016). Hemiparesis is the most common neurological abnormality that occurs after a patient sustains penetrating head injuries (Muballe *et al*., 2016). A significant proportion of TBI in SA occurs as a consequence of penetrating injuries (Buitendag *et al*., 2019). Penetrating TBI in paediatrics is uncommon. However, it may be caused by pens, needles, nails, and other sharp objects (Muballe *et al*., 2016).

TBI may result in diffuse injury or focal injury. Diffuse TBI has minimal surgically treatable lesions (sub-arachnoid bleeds, pin-point haemorrhages or diffuse brain oedema and sometimes multiple contusions), while focal brain injury includes both surgically treatable lesions (extradural or subdural haematoma, intracerebral bleeds) or non-surgical lesions (smear subdural and large contusions) (Huffman *et al*., 2004). Focal TBI typically results from a force to the head that may result in cerebral contusions or hematomas. Mortality and morbidity depend on the site, size, and progression of the injury (Huffman *et al*., 2004). Intracranial bleeding is a frequent and life-threatening repercussion of TBI. Perel and colleagues state that 56% of patients with TBI presented with intracranial bleeding (Perel *et al*., 2009). Intracranial bleeding is categorised as epidural haemorrhage (EDH), subdural haemorrhage (SDH), intraparenchymal haemorrhage (IPH) and subarachnoid haemorrhage (SAH) (Perel *et al*., 2009). A large study with more than 13 000 patients revealed a significant increase in mortality rate in patients with a large EDH, SDH or IPH (Perel *et al*., 2009).

Epidural Hematoma

The epidural space is the area between the inner part of the calvarium and the dura (Abdelmalik *et al*., 2019). There is a firm attachment between the dural layer and the inner part of the skull. Therefore, there is no real space present. An epidural hematoma (EDH) usually occurs from injury to the anterior or middle meningeal artery or its branches (Abdelmalik *et al*., 2019). EDHs are recognised on CT scan imaging as a hyperdense lens-shaped opacity within the epidural space (Abdelmalik *et al*., 2019). EDH occurs when a fracture of the temporal bone damages the middle meningeal artery resulting in the accumulation of blood into the epidural space (Abdelmalik *et al*., 2019). EDHs may present with a lucid interval and a sudden decrease in sensorium (Abdelmalik *et al*., 2019). EDH is an emergency and requires acute surgical intervention. EDH is associated with a good outcome if the appropriate intervention is

performed before brain herniation or local compression occurs (Abdelmalik *et al*., 2019). EDH is usually performed within 4-6 hours post-injury.

Subdural hematoma

A subdural hematoma occurs when there is haemorrhaging between the meningeal layer of the dura and the arachnoid layer. SDH usually occurs because of an injury to the superficial cortical veins. The SDH begins to push the arachnoid away, which results in the stretching of the bridging veins. Eventually, this will result in venous rupture, causing a further accumulation of SDH (Abdelmalik *et al*., 2019). Often the brains of geriatric patients have age-related atrophy, and their cortical veins are stretched. Therefore, a minor injury to the head can tear the veins resulting in low-pressure haemorrhaging and the accretion of blood within the dura and arachnoid layers (Abdelmalik *et al*., 2019), which is made worse if they are taking aspirin or other anticoagulants. Approximately 10% of subdural hematomas are related to EDH (Anzai and Minoshima, 2011). SDHs are recognised on CT scan imaging as a hyperdense bleed into the subdural space that flows over the surface of the brain (Kulesza *et al*., 2020).

Diffuse axonal injury

Diffuse axonal injury (DAI) presents as minor spotted haemorrhages that result from shear forces during brain movement (Abdelmalik *et al*., 2019). DAI is distinguished by axonal stretching, disruption and, ultimately, separation of the nerve fibres (Xu *et al*., 2007). It is often associated with decreased GCS score and sudden onset of a comatose state (Xu *et al*., 2007). Changes in consciousness were primarily attributed to brainstem injury (Su and Bell, 2016). However, axonal damage in the white matter of the brain is often associated with DAI (Su and Bell, 2016). Magnetic resonance imaging is the neuroimaging method of choice for suspected DAI (Abdelmalik *et al*., 2019).

Cortical contusions

Cortical contusions occur in the areas where the brain makes contact with the inner part of the skull (inferior, frontal or temporal lobes) (Abdelmalik *et al*., 2019). Cortical contusions often involve haemorrhage as a result of vascular damage and are often aggravated with resuscitation (Abdelmalik *et al*., 2019). Subsequent to traumatic brain

injury, the maximal risk is within the initial nine hours of injury (Abdelmalik *et al*., 2019). Generally, these lesions progress before slowly regressing.

2.6 Outcome predictors

Predicting patient outcome has enabled healthcare providers to anticipate the improvement or deterioration of a patient's condition. Studies performed that utilised datasets from the International Mission on Prognosis and Analysis of Clinical trials (IMPACT) in traumatic brain injury have indicated an important ranking of admission variables (Raj *et al*., 2014). The most influential predictors of clinical outcome are as follows:

- Demographics – Demographics include the age, sex, and ethnic origin of the patient.
- Glasgow Coma Scale – The patients' initial level of consciousness plays a crucial role in predicting patient outcome.
- Arterial Hypotension – Hypotension is defined as systolic blood pressure below 90mmHg.
- Pupil Response – Pupil reaction to light and size of both pupils assists with determining the severity of neurologic damage.
- Computer Tomography (CT) Scan – CT scans allow healthcare providers to determine underlying injuries and confirm injuries such as herniation of the brain stem. Literature suggests that the Marshall CT classification indicates that patients with diffuse brain injury had favourable outcomes while patients with a Marshall's CT classification grouped as IV or V having a mass lesion had unfavourable results (Rincon-Guio *et al*., 2017).

Vital signs are utilised to monitor the body's primary functions. During a traumatic incidence, TBI may result in dysautonomia, which occurs in 10% of patients who survive despite having a poor outcome. Dysautonomia presents with alterations in blood pressure, pulse rate, respiratory rate, temperature, muscle tone, decorticate positioning, decerebrate posture and diaphoresis. Additional components that are variable predictors for poor outcome of TBI, include injury severity score (ISS), absent pupillary response, hypotension/hypertension, increase in intracranial pressure (ICP), hypoxia, hypoglycaemia/hyperglycemia, hypothermia/hyperthermia, decreased haemoglobin levels, coagulopathy, raise in lactate levels, electrolyte abnormalities,

high Marshall's CT classification as well as epidural, subdural and subarachnoid haemorrhage in the brain (Rincon-Guio *et al*., 2017)**.**

Davis *et al.* (2004) concluded a significant increase in mortality in patients with a partial pressure of oxygen (pO2) < 70mmHg and end-tidal carbon dioxide (EtCO2) < 27mmHg (Davis *et al*., 2004). This study also observed that patients with EtCO2 < 25mmHg for a mean duration of six minutes (390 seconds) might have adverse effects on the brain, such as cerebral vasoconstriction, reduced cerebral blood flow and increased intrathoracic pressure (Davis *et al*., 2004). An association between an increase in mortality rate and hypocapnia was identified (Davis *et al*., 2004). Hypocapnia may occur as a result of increased ventilatory rates (Davis *et al*., 2004) and this has resulted in the recommendation for the use of normocapnia in TBI management.

Demographics

Trauma-related injuries, including traumatic brain injury, are more frequent in males compared to females. Studies show better outcomes in females may result from the neuroprotective effect of progesterone (Kulesza *et al*., 2015). Poor patient outcome is directly related to increasing age, especially in patients older than 40 and 60 years of age. This is likely because of extracranial comorbidities, alterations in cerebral plasticity or changes in the clinical management of older patients (Kulesza *et al*., 2015).

Glasgow Coma Scale

Various clinical tools are available to categorise the severity of traumatic brain injury, including radiographic and clinical tools such as Marshall CT classification and Glasgow Coma Scale (Abdelmalik *et al*., 2019). The Glasgow Coma Scale is simple, durable and broadly utilised by healthcare providers (Abdelmalik *et al*., 2019). The Glasgow Coma Scale was introduced by the Glasgow working group in 1974 and has become a common scale to determine a patient's level of consciousness and neurological functioning that can be simply liaised with other clinical healthcare workers (Singata and Candy, 2018). In 1974, GCS was designed to determine any change in patient condition and to measure the "duration of coma" within the first two days in neurosurgical units (Raj *et al*., 2014). GCS consists of three components: eye opening, verbal response and best motor response. The three components added

together produce a score between 3-15. GCS assessment in the pre-hospital environment is a crucial and dependable criterion of the severity of TBI, especially in identifying any improvement or deterioration of GCS post-injury (Badjatia *et al*., 2008). GCS should be assessed after airway, breathing and circulation are assessed and maintained (Badjatia *et al*., 2008). GCS may be influenced by traumatic factors that may be reversed by EMS personnel, such as hypoglycaemia and narcotic misuse (Badjatia *et al*., 2008). Clinical subjectivity and the inability to assess the verbal component after intubation produces limitations to the GCS tool. GCS is the most common scale utilised to assess a patient's levels of consciousness (Moppett, 2007). However, GCS has a shortcoming in patients where eye opening and verbal and motor responses are affected by trauma, oedema and intubation (Moppett, 2007).

Glasgow Outcome Scale

The Glasgow Outcome Scale (GOS) was initially established in 1975 by Jennett and Bond to encompass parts of crucial life tasks utilising a scale of 1 to 5 to categorise overall disability post-traumatic brain injury (Mahadewa *et al*., 2018). GOS is the gold standard for assessing the longer-term outcome of traumatic brain injury in adults. The Glasgow Outcome Scale Extended (GOSE) increases sensitivity from the GOS to particular deficits, with each category ranging from 1-8 (Mahadewa *et al*., 2018). The Glasgow Outcome Scale may be utilised to assess the prognosis following traumatic brain injury. Table 2 represents the categories of the Glasgow Outcome Scale Extended.

Table 2: Glasgow Outcome Scale extended

Score	Glasgow Outcome Score Extended (GOSE)	Description
1	Dead (D)	
2	Vegetative State (VS)	Patient exhibits no obvious cortical function
3	Lower Severe Disability (SD-)	Able to follow commands, needs help with all activities, unable to live alone
4	Upper Severe Disability (SD+)	Able to follow commands, needs help with most activities; unable to live alone.
5	Lower Moderate Disability (MD-)	Able to live independently requires some assistance, unable to return to work or school
6	Upper Moderate Disability (MD+)	Able to live independently requires little assistance, unable to return to work or school.
7	Lower Good Recovery (GR-)	Able to return to work or school with mild difficulty
8	Upper Good Recovery (GR+)	Able to return to normal activities

Arterial Hypotension and Hypoxia

Hypotension is defined as systolic blood pressure (SBP) < 90mmHg in adults (Kulesza *et al*., 2015). Favourable outcomes are associated with systolic BP between 90mmHg and 135mmHg. Any systolic BP not within those ranges is associated with unfavourable patient outcome (Kulesza *et al*., 2015). Protocols for identifying and treating secondary insults such as hypoxemia and hypotension are associated with improved outcome in TBI (Geeraerts *et al*., 2018). The correlation between arterial pressure and patient outcome is best illustrated by systolic blood pressure ≤ 90mmHg during the initial patient management and resuscitation. Systolic BP measurement is relatively uncomplicated and precise in the field. However, SBP does not accurately predict the mean arterial pressure (MAP). Poor patient outcome is directly related to systemic hypotension. One hypotensive event is associated with an increase in morbidity and almost twice the mortality rate (Moppett, 2007). The frequency and quantity of hypotensive events correlate with the rate of mortality (Moppett, 2007). Hypoventilation and hyperventilation have also shown to be associated with poor patient outcome (Kulesza *et al*., 2015). Severe TBI patients should be continuously monitored for hypoxemia (arterial haemoglobin oxygen saturation <90% and hypotension (systolic BP <90mmHg) (Marehbian *et al*., 2017).

Pupillary response

Studies yield a significant correlation between abnormal and absent pupillary response and poor patient outcome in traumatic brain injury (Kulesza *et al*., 2015). Abnormal pupillary reaction is frequently associated with severe TBI and a decreased GCS score (Brennan *et al*., 2018). Abnormal pupillary response is more common in patients with mass lesions, compressed cisterns, shift and Marshall CT class III/IV compared to TBI patients with CT class I/II (Kulesza *et al*., 2015). Pupil examination must be performed after resuscitation and stabilisation due to metabolic and/or cardiovascular chances that result in hypoxemia, hypotension, and hypothermia, which will cause pupillary response (Badjatia *et al*., 2008). Pupil assessment includes the examination of bilateral pupils for unilateral/bilateral dilation and fixed pupils. Asymmetry is determined by > 1mm variance in pupil size. A fixed pupil is determined by < 1mm response to external stimuli (Badjatia *et al*., 2008). The pupillary response assessment involves an examination of the pupil's size, symmetry, and reaction to external stimuli such as light (Badjatia *et al*., 2008). The pupillary light reflex relies on the adequate function of the third cranial nerve, lens, retina, optic nerve, and brain stem (Badjatia *et al*., 2008).

CT Scan

Computed tomography of the brain is the method of choice for the initial analysis of a TBI. The cranial CT is sensitive and allows for the recognition of acute haemorrhagic lesions that may require surgical intervention. It also provides more extensive details. Lemcke *et al.* (2009) discovered a significant correlation between patient outcome and midline shift identified on a CT scan post decompressive craniectomy. Patients with a Glasgow Outcome Scale of 1-3 (poor outcome) presented with a mean midline shift of 9.8 +- 6.7mm. Patients with a GOS of 4-5 (good outcome) presented with a mean midline shift of 6.7mm +- 5.0mm. The identification of basal cisterns was also shown to be significantly associated with the quality of patient outcome (Rincon-Guio *et al*., 2017).

2.7 Management of traumatic brain injury patients

Reducing mortality and morbidity in patients with severe traumatic brain injury (TBI) is beneficial to society and citizens because of the management, long-term rehabilitation and financial costs incurred (Bossers *et al*., 2020). Mortality and morbidity of traumatic brain injury are directly related to increased intra-cranial pressure (ICP), haemorrhagic

contusion and cerebral oedema (Abdelmalik *et al*., 2019). Enhancement in emergency medical care has been shown to have resulted in a reduction in the mortality rate in patients who sustained a TBI (Tobi *et al*., 2016). Pre-hospital patient treatment protocols should aim to prevent and treat causes of secondary brain injury such as hypoxia, hypotension, hypoventilation and hyperventilation (Bossers *et al*., 2020). After the initial traumatic brain injury, brain damage may be aggravated by secondary insults such as hypotension, hypoxia and raised ICP (Gravesteijn *et al*., 2021). Pre-hospital patient treatment aims to prevent secondary TBI by stabilising the patient on-scene and providing rapid transportation to hospital (Gravesteijn *et al*., 2021). However, on-scene stabilisation can delay time to hospital where essential diagnostic treatment is performed, worsening patient outcome (Gravesteijn *et al*., 2021). Other studies, however, indicate that on-scene stabilisation prior to transportation to distant specialist facilities may improve patient outcome (Gravesteijn *et al*., 2021). Pre-hospital healthcare personnel decide whether to stabilise patients on-scene or immediately transport the patient to the closest appropriate facility. This decision is based on the patient's clinical condition, injuries, level of qualification of healthcare workers and local policy (Gravesteijn *et al*., 2021) and may be influenced by distance to the receiving facility. Although the national European guideline for pre-hospital management of TBI is easily available, patients continue to arrive at ED with hypotension and hypoxia occurring in 13% and 7% of patients, respectively (Gravesteijn *et al*., 2021). The principal predictor of this physiological instability were due to significant extracranial injuries (Gravesteijn *et al*., 2021).

On-scene stabilisation in the pre-hospital environment that involves advanced medical interventions may result in a time delay in arriving at the appropriate hospital (Gravesteijn *et al*., 2021). The main reason for delayed time on-scene were interventional and situational rather than patient-associated reasons (Gravesteijn *et al*., 2021). Various factors influence on-scene time due to the nature of the pre-hospital environment (Vincent-Lambert and Mottershaw, 2018).

These factors can be categorised into three sections:

- Environmental: weather, time, entrapments etc., (Vincent-Lambert and Mottershaw, 2018).
- Clinical: pre-hospital medical interventions such as airway management and medicine administration (Vincent-Lambert and Mottershaw, 2018).

- Systemic: ambulance accessibility, pre-hospital personnel arrangements and method of transportation (Vincent-Lambert and Mottershaw, 2018)

Pre-hospital patient management, including intubation, intravenous fluid administration and helicopter transportation, is reliant on the country where the patient was injured (Gravesteijn *et al*., 2021). Increased time spent on-scene can be explained by pre-hospital interventions such as pre-hospital intubation. This delay in transportation to appropriate medical care may worsen patient outcome (Raj *et al*., 2013). However, some studies reveal improved patient outcome in patients stabilised on-scene prior to transportation to a trauma facility (Gravesteijn *et al*., 2021). In Europe, on-scene time increased by ten (10) minutes due to pre-hospital intubation, whereas other interventions, such as intravenous access and mechanical ventilation, increased time spent on-scene slightly (Gravesteijn *et al*., 2021).

The guidelines for pre-hospital management of Traumatic Brain Injury 2nd edition by Badjatia and colleagues (2008) are older but are still supported by current literature, such as the clinical practice guidelines published by the Health Professions Council of South Africa (HPCSA). The Brain Trauma Foundation pre-hospital guidelines for the management of traumatic brain injury (TBI) suggests assessing the patients initial Glasgow Come Scale (GCS) and pupillary size; a targeted systolic blood pressure > 90mmHg; oxygen saturation > 90% and fast triage to a trauma facility (Marehbian *et al*., 2017). The majority of the world-wide guidelines for the management of head injury include pre-hospital management (Ammar, 2018). The BTF pre-hospital guideline states:

- A common, effectual, and available network of communication.
- An initial in-depth patient examination including:

Airway – Ensuring that the airway is secured and ensuring appropriate oxygenation. The BTF pre-hospital guidelines for TBI recommend establishing a secure airway in patients unable to protect their airway (GCS < 9) and in patients with oxygen saturation levels < 90% despite the administration of supplemental oxygen (Marehbian *et al*., 2017). Rapid sequence intubation by ALS paramedics in TBI patients is associated with better neurologic outcomes at six months compared to delayed intubation until arrival at a trauma facility (Marehbian *et al*., 2017). Routine rapid sequence intubation is not recommended in patients with spontaneous respiratory effort and oxygen

saturation > 90% on oxygen therapy (Badjatia *et al*., 2008). Advanced airway management is recommended in patients with severe traumatic brain injury (GCS < 8) unable to adequately maintain their airway and hypoxemia unresolved by supplemental oxygen (Rubenson Wahlin *et al*., 2018). A normal respiratory rate (12-20bpm) must be maintained with normal end-tidal CO2 (EtCO2) ranging from 35-40mmHg (Badjatia *et al*., 2008). Airway management and oxygenation are crucial in TBI in the pre-hospital environment (Badjatia *et al*., 2008). Endotracheal intubation is required when respiratory and/or cardiac arrest is likely to occur (Jung, 2015). Severe hemodynamic changes often occur as a consequence of intubation, and a risk-benefit analysis should be considered prior to intubation (Jung, 2015). The use of capnography is the most reliable method to monitor the ventilatory rate and confirm endotracheal tube position (Price *et al*., 2020). Hyperventilation results in hypocapnia, defined as PaCO2 <35mmHg, associated with poor patient outcome (Badjatia *et al*., 2008), on the basis of cerebral ischemia.

Breathing – Assess respiratory rate, rhythm, and depth. Adequate ventilation relies on the rate of ventilation, tidal volume and the pressure applied to administer a set tidal volume (Badjatia *et al*., 2008). If capnography monitoring is not possible, monitoring of chest rise and proper airway seal is recommended (Badjatia *et al*., 2008). Ventilation rates of 10-20bpm at 6-7mL/kg are suggested to reduce gastric inflation, adjusted to end-tidal CO2 (Hardcastle *et al*., 2017). Exclusion of chest injury is also essential.

Circulation – The goal in trauma patients is to assess the patients' pulse, blood pressure and capillary refill to prevent and treat shock. It is crucial to recognise the site of haemorrhage, which can result in hypotension and stop the bleeding. As mentioned earlier, hypotension is a reliable predictor of mortality in TBI, with even one hypotensive event being associated with double mortality and increased morbidity (Marehbian *et al*., 2017). Accordingly, fluid administration is crucial in the prevention and management of secondary injury that occurs post-injury and affects neurological recovery (Roquilly *et al*., 2021). In the pre-hospital environment, fluid resuscitation is vital in the treatment of TBI patients (Bergmans *et al*., 2020).

Often, trauma leads to reduced cardiac pre-load caused by bleeding. When the body's compensatory mechanisms fail, hypovolemia results in reduced peripheral perfusion and oxygenation. Isotonic fluids are recommended to treat patients with systolic blood

pressure (SBP) < 90mmHg (Badjatia *et al*., 2008). The use of isotonic crystalloid fluids is commonly administered in the pre-hospital environment, although there is insufficient data to support its use (Badjatia *et al*., 2008). Fluid resuscitation in the pre-hospital environment aims to promote oxygenation and improve cerebral dynamics. Crystalloid fluids are often administered to increase cardiac pre-load, preserve cardiac output and adequate oxygenation. In adult patients, a maximum of 1L isotonic solution should be administered. If unresponsive to the crystalloid fluid bolus, a blood transfusion is recommended (Henry, 2018). Cerebral autoregulation is frequently compromised in TBI. As a result, the regional cerebral blood flow (CBF) relies on systemic blood pressure. A systolic BP >=100mmHg in patients between 50-69 years of age and a systolic BP of 110mmHg in patients between 15-49 years of age or older than 70 years of age is recommended by the 2016 BTF guidelines (Abdelmalik *et al*., 2019). Norepinephrine and phenylephrine are the drugs of choice in TBI since they have a minimal effect on the cerebral vasomotor tone (Abdelmalik *et al*., 2019).

There are no pre-hospital guidelines that exist regarding the treatment of intracranial hypertension (Bergmans *et al*., 2020). Hypertonic saline and Mannitol are often used to treat intracranial hypertension in emergency departments and intensive care units, not in the pre-hospital environment. A study performed by Bergmans and colleagues did not identify improved neurological outcome or higher survival in patients treated with hypertonic saline (Bergmans *et al*., 2020). Another study did not reveal improved or better neurological outcome at six months in patients resuscitated with hypertonic fluid after TBI (Bulger *et al*., 2010). Isotonic fluids are the fluid of choice in managing hypotension in TBI patients. However, hypertonic fluids in patients with GCS< 8 are recommended as an option (Marehbian *et al*., 2017). Hyperosmolar fluids are extensively used to control intracranial pressure (ICP) (Berger-Pelleiter *et al*., 2016). Mannitol is the most commonly used hyperosmolar solution and is considered gold standard treatment of raised intracranial pressure (Berger-Pelleiter *et al*., 2016). However, mannitol solutions consist of diuretic properties which might cause volume depletion, hypotension and reduced cerebral perfusion (Berger-Pelleiter *et al*., 2016).

Disability – Assess Glasgow Coma Scale (GCS) and pupils for equal reaction and light reflexes.
Expose – Examine the chest, abdomen, and limbs.

- Ensure cervical spine stabilization by applying spinal motion restriction.

Spinal injuries often occur in conjunction with traumatic brain injury and it should be assumed that all patients who sustained a traumatic brain injury and presented with an altered mental status or blunt injury above the clavicle have sustained a cervical spinal injury (Abdelmalik *et al*., 2019). The use of cervical collars as part of a management protocol for cervical spine injuries is no longer recommended due to the multiple adverse effects of cervical collars, such as an increase in intracranial pressure, increasing movement in unstable fractures, tissue necrosis and patient discomfort (Stanton *et al*., 2017).

All patients with a decreased GCS require cervical spine investigation (Malale *et al*., 2020). Cervical spine injuries (CSI) are associated with a high morbidity rate and often occur in conjunction with TBI (Malale *et al*., 2020). Although there is minimal evidence available in South Africa regarding TBI combined with CSI, treatment guidelines suggest a CT scan of the brain and spine in a patient with blunt trauma injury and a decreased GCS (Malale *et al*., 2020).

- Insert a chest drain in patients with a pneumothorax, haemothorax or hemopneumothorax.
- All patients with a GCS of less than 9 qualify for intubation and should be intubated at the site of injury.
- Bilateral intravenous lines should be established. The goal is to maintain adequate blood pressure and circulation, control intracranial pressure and prevent cerebral oedema. Currently, there is insufficient evidence to support the worsening of cerebral oedema due to large fluid administration in patients with a compromised blood-brain barrier function (Moppett, 2007). A study performed by Vassar and associates established no increase in the rate of bleeding in patients who were administered hypertonic saline (Moppett, 2007).
- Provide adequate sedation. The use of sedatives is crucial to prevent or manage intracranial hypertension and seizures (Purbhoo, 2018). Anaesthetics and sedatives prevent unwanted movements, coughing, tension against tubes, metabolic suppression and changes in cerebral vascular tone (Purbhoo, 2018).
- Early appropriate brain and spinal imaging and the application of the Tiered Treatment approach are also recommended.

The BTF guidelines suggest the administration of specific medication upon arrival at the emergency department (ED) to assist with the prevention of intracranial haemorrhage in severe TBI. Tranexamic acid (TXA) is classified as an antifibrinolytic capable of preventing excessive blood loss. TXA has shown a reduction in mortality rate in trauma patients. However, it may be detrimental if administered beyond three hours post-traumatic event (Marehbian *et al*., 2017).

Intracranial Pressure

CPP=MAP-ICP

Any rise in intracranial pressure (ICP) results in a decrease in cerebral perfusion pressure (CPP), risking ischemia (Khellaf *et al*., 2019). An ICP of less than 20-25mmHg is the goal value in traumatic brain injury (Khellaf *et al*., 2019). ICP monitoring is associated with a decrease in both in-hospital and two-week post-traumatic brain injury mortality rate (Abdelmalik *et al*., 2019). According to Abdelmalik *et al.* (2019), an ICP > 22mmHg is associated with a higher mortality rate. The best practice for ICP monitoring is the insertion of an external ventricular drain (EVD), where a catheter is placed into the third cerebral ventricle (Abdelmalik *et al*., 2019). An EVD also assists with the management of intracranial hypertension and cerebral spinal fluid elimination (Abdelmalik *et al*., 2019). The use of an anti-microbial impregnated EVD catheter might decrease the risk of developing ventriculitis (Abdelmalik *et al*., 2019). CPP depicts the pressure distributing oxygen and glucose to the brain (Abdelmalik *et al*., 2019). A CPP of 60-70mmHg is suggested in severe TBI. A CPP value higher than 70mmHg is not recommended (Abdelmalik *et al*., 2019).

Cerebral Herniation

Neuronal injuries may be caused by primary injuries such as direct trauma or by secondary injuries caused by hypoxemia, hypotension, and cerebral oedema (Badjatia *et al*., 2008). The treatment objectives in TBI are to maintain cerebral perfusion and decrease neuronal injury. Fixed pupils, asymmetric pupils, extensor posturing or the continuous decrease in the level of consciousness suggests cerebral herniation and should be frequently evaluated (Badjatia *et al*., 2008). In patients with cerebral herniation or neurologic deterioration, hyperventilation may be required. Hyperventilation results in cerebral vasoconstriction, subsequently causing a decrease in cerebral blood flow. Hyperventilation decreases intracranial pressure in

patients presenting with cerebral oedema (Badjatia *et al*., 2008). Hyperventilation occurs when EtCO2 ranges 30-35mmHg and may be achieved by providing 20 breaths per minute in adults. It is to be used as a “bridge” to surgical intervention. This technique should be used in patients who are effectively oxygenated at normal ventilatory rates and normal blood pressures (Badjatia *et al*., 2008). The standard treatment for cerebral herniation involves positioning the head at a 30° angle, hyperventilation, and either mannitol diuresis or hypertonic saline (Abdelmalik *et al*., 2019). Correct head positioning encourages venous drainage, reducing intracranial venous blood and, thus, decreasing intracranial pressure (Abdelmalik *et al*., 2019). Mannitol is not recommended by the 2016 BTF guidelines due to insufficient clinical evidence to support its use (Abdelmalik *et al*., 2019). Hypertonic saline increases serum osmolarity without affecting intravascular volume. A serum osmolarity of 300-320 mOSM/L is considered the goal treatment in patients. Hypertonic saline may reverse brain herniation, decrease ICP and increase CPP (Abdelmalik *et al*., 2019).

Imaging

Computed tomography (CT) scan and on selected patients, magnetic resonance imaging (MRI), of the brain is used to diagnose traumatic brain injury. Computed tomography scan remains the method of choice to categorise patients according to those who require emergent surgical intervention or conservative medical treatment in the emergency setting (Rincon-Guio *et al*., 2017). CT scan is the brain imaging of choice because it is efficient, widely accessible and precise in the identification of cranial fractures and intracranial lesions, including haemorrhages, herniation, and hydrocephalus. In some instances, these intracranial lesions may require immediate surgical intervention (Rincon-Guio *et al*., 2017). The fundamental function of CT scans is the rapid identification of focal injuries of the brain that may require rapid neurosurgical intervention. Approximately 10% of severe TBIs require a craniectomy based on the initial CT scan identification, including extra-axial hematomas greater than 30mL or linked associated with a midline shift more than 5mm and parenchymal hematomas in a non-eloquent cortex larger than 20mL (Rincon-Guio *et al., 2017)*. Raised ICP is indicated by a midline shift of the brain and is associated with poor patient outcome. Patient mortality is lower in patients with an epidural haematoma compared to patients with an acute subdural haematoma (Rincon-Guio *et al*., 2017). Approximately 90% positive predictive value for a poor patient outcome is associated

with intracranial haemorrhages (Rincon-Guio *et al*., 2017). The Marshall CT classification is one of the most used methods to determine morbidity and mortality by assessing tomographic patterns of injury, including diffuse and focal injuries (Rincon-Guio *et al*., 2017). The Marshall classification is limited in polytrauma patients, and it is not linear, making it difficult to use to define severity (Rincon-Guio *et al*., 2017). This is a valid instrument to determine the midline shift, local mass lesion and mesencephalic cisterns (Rincon-Guio *et al*., 2017). The table below depicts the mortality associated with each Marshall CT scan classification.

Table 3: The Marshall CT Classification

	Diffuse Injury I	Diffuse Injury II	Diffuse Injury III	Diffuse Injury VI	Evacuated Mass Lesion	No evacuated Mass Lesion
Definition	No visible pathology	Cisterns present with midline shift </=5 mm Lesion densities present. No high or mixed density lesion >25 cc	Cisterns compressed/ absent with midline shift </=5 mm No high or mixed density lesion >25 cc	Midline shift >5 mm No high or mixed density lesion >25 cc	Lesions surgically removed	Any high or mixed density lesion >25 cc is not surgically removed
Mortality	10%	14%	34%	56%	39%	53%

2.8. Hospital capabilities in South Africa

Hospitals are placed into different trauma categories depending on the hospitals' capabilities to manage trauma patients, as defined by the Trauma Society of South Africa criteria (Hardcastle *et al*., 2011). This system is beneficial to patients because trauma cases are managed by the entire emergency and surgical team, and there is an audit of the outcome, ultimately improving patient management.

2.8.1 Level I

A level I trauma facility is a major trauma referral centre. It should contain all the resources required to treat all types of injuries, prevention of injuries and rehabilitation, and 24-hour availability of all major specialities (Hardcastle *et al*., 2011).

2.8.2. Level II

A level II facility is an urban trauma centre established to administer initial medical care irrespective of the severity of the patient's injuries (Hardcastle *et al*., 2011). This facility operates 24 hours to provide definitive medical care, including common specialities such as general surgery, orthopaedic surgery, neurosurgery, radiology, and emergency medicine, plus those specified in the TSSA accreditation template. In situations where a level II facility is unable to provide comprehensive care (due to inadequate resources, increased patient volume and the geographical location of the hospital), they may be transferred to a level I facility where they can receive advanced and extended surgical critical care. In locations where there is no level I facility available, a level II facility is required to provide education and system leadership.

2.8.3 Level III

A level III facility is a community hospital that can provide rapid patient assessment, resuscitation, patient stabilisation and basic operations. A level III facility provides medical care to citizens who are unable to access a level I or level II facility immediately. These patients may later be transferred to a level I or level II facility to receive definitive medical care. These facilities must have readily accessible general surgeons or general practitioners with surgical expertise. Prompt transfer systems and standardised protocols are necessary to plan for the medical treatment of patients (Hardcastle *et al*., 2011).

2.8.4 Level IV

A level IV facility is a primary healthcare facility where patients treated at this facility receive basic trauma life support and after that are referred to a more appropriate facility where definitive medical care is provided (Hardcastle *et al*., 2011). Therefore, it is vital for a level IV facility to communicate well with other trauma centres.

2.9 Emergency medical services

In 1877, the first ambulance service to be established in South Africa was known as the St John Ambulance Brigade (Van Huyssteen, 2016). First aiders were of vital importance and assisted with casualties and disease in the South African war that took place in 1899 (Van Huyssteen, 2016). As time went by, the emergency medical services (EMS) system continued to grow. The EMS capabilities became more advanced, and the purpose of an ambulance became significant (Van Huyssteen, 2016). The EMS system in South Africa has evolved over the past two decades, yet there remains to be an unequal distribution of EMS, particularly in poorly resourced rural areas (Macfarlane *et al*., 2005).

There are currently three levels of EMS personnel training levels namely basic life support (BLS), intermediate life support (ILS) and advanced life support (ALS). Advanced life support personnel are greatly comparable worldwide (Macfarlane *et al*., 2005). Traditionally, pre-hospital management involved a 'scoop and run' strategy. A 'stay and play' method is the preferred strategy where ALS management is recommended in the 20th century (Aubuchon *et al*., 2013). Advanced life support capabilities include BLS and ILS capabilities, including more invasive procedures such as endotracheal intubation and drug administration (Aubuchon *et al*., 2013).

All EMS personnel require registration with the Health Professionals Council of South Africa and comply with their scope of practice, regulations, and disciplinary structures (Macfarlane *et al*., 2005). South Africa utilises the Anglo-Saxon model, a paramedic-based model where doctors rarely practice in the pre-hospital environment (Van Huyssteen, 2016).

2.10 Pre-hospital Triage

EMS personnel are required to perform initial patient assessment and management of injured patients in the pre-hospital environment. They play an important role in the triage of these patients to the pertinent/relevant healthcare facility (Mccoy *et al*., 2013). The triage of injured patients to the relevant medical facility is crucial for patient outcomes (McCoy *et al*. 2013). A remarkable 25% relative risk reduction in mortality of severely injured adult patients who were treated at a level 1 trauma centre compared to a non-trauma centre was recognised by the National Study on the Costs and Outcome of Trauma. The Brain Trauma Foundation guidelines for pre-hospital care

suggest patients who sustain a severe TBI should be transported directly to a facility with CT scan capabilities, neurosurgical care and ICP monitoring capabilities (Marehbian *et al*., 2017). The mortality and morbidity weekly report on the guidelines for field triage of injury patients discusses the four steps of the triage process.

Step one: Physiologic Criteria

Step one includes rapid recognition of critically injured patients by evaluating their level of consciousness (GCS) and the assessment of their initial vital signs. Crucial predictors of severe TBI include a systolic BP < 90mmHg and a respiratory rate < 10 bpm or a respiratory rate > 29 bpm. Patients with these predictors require a higher level of care (McCoy *et al.* 2013:70). The guidelines for field triage of injured patients recommend direct transportation to a healthcare facility with the highest level of care in the defined trauma system if the patient presents with GCS<13, SBP < 90mmHg and a respiratory rate < 10bpm or >29bpm.

Step two: Anatomic criteria

The guideline identifies that some patients may appear to have normal physiology but have an anatomic injury requiring the highest level of care within the defined trauma system (Mccoy *et al*., 2013). The criteria include:

- All patients with penetrating injuries to the head, neck, torso, and injuries proximal to the elbow or knee.
- Patients presenting with a flail chest.
- Patients who sustained a crushed, degloved, mangled or pulseless extremity.
- Amputation proximal to wrist or ankle

Step three: Mechanism of injury

Patients who do not fall within the physiologic and anatomic criteria require evaluation of the mechanism of injury to establish the severity of the injury (Mccoy *et al*., 2013). If a patient meets the following criteria, it is recommended to transport the patient to the relevant trauma facility:

- Fall from height > 6 meters for adults and > 3 meters in children.
- High-risk auto crash, including roof intrusion > 30cm on the patients' site, ejection from vehicle, and death of a passenger in the same section of the vehicle.

- Vehicle data associated with high injury risk.
- Collision involving a vehicle and a pedestrian or a cyclist.
- Motorcycle crash > 32km/hr.

Step four: Special considerations

In this step, medical personnel should identify patients who have not met the physiologic, anatomic or mechanism of injury criteria and have other medical conditions or factors that will increase their risk of injury or assist in recognising the critically injured patient (Mccoy *et al*., 2013). The 'older adults' criterion was changed to assist in identifying that a systolic blood pressure < 110mmHg may indicate shock in elderly patients older than 65 years of age, and low impact mechanism of injury may lead to severe injuries (Mccoy *et al*., 2013). In older patients, there is a high risk for rapid deterioration with head injury on anticoagulation therapy or known bleeding disorders, end-stage renal disease and time-sensitive extremity injury (Mccoy *et al*., 2013).

Other triage systems exist locally, such as the South African Triage Scale (SATS), which was constructed to triage patients arriving at facilities in poor-resourced African environments (Dixon *et al*., 2021). The final SATS score is determined after assessing factors such as heart rate, respiratory rate, SBP, mobility, temperature, GCS and the presence of trauma (Dixon *et al*., 2021). According to the Western Cape Government, the South African Triage Scale has five priority levels, namely:
Red: Red code patients require immediate patient management.

Orange: An orange code requires patient management within 10 minutes. It requires 'VERY URGENT' management.

Yellow: A yellow code requires patient management within one hour. It requires 'URGENT' management.

Green: A green code requires patient management within four hours. It is regarded as 'non-urgent'.

Blue: A blue code refers to a deceased person. It requires a referral to a doctor for certification.

2.11 Conclusion

This chapter reviewed relevant literature on traumatic brain injury, outcome predictors, patient outcome, and patient management focusing on pre-hospital management and transportation methods to the hospital. While traumatic brain injury remains a high cause of mortality and morbidity in South Africa, designated trauma systems equipped to manage traumatic brain injuries are scarce, and pre-hospital providers are required to make efficient patient management and transportation decisions on-scene. It was evident from the literature reviewed that there are important variables associated with TBI to predict patient outcome. It is critical that all healthcare workers understand the importance of preventing secondary brain injury by providing appropriate treatment, rapid transportation to the relevant facility and by determining patient outcome.

Chapter 3

Research Methodology and Design

3.1 Introduction

The purpose of this chapter is to discuss the research process utilised during the study by describing the data collection process, data validation and data analysis. The research design and research methodology are discussed extensively, including the ethical considerations required to begin this study, such as study setting, data collection, population, sampling techniques and data validity. Research methodology is the path to conduct research. It reveals the path in which researchers compose the research problem, and objective and indicate the results obtained during the study period (Jilcha Sileyew, 2019). This chapter also includes outlines of inclusion criteria and data collection methods (primary and secondary data collection).

3.2 Research design

The research design aims to produce a framework for a research study (Jilcha Sileyew, 2019). The research approach is a very significant decision in the research design process as it influences the data collection process. This study utilised a descriptive research design to describe various patient outcomes in severe traumatic brain injury in patients admitted to a level 1 trauma centre. The researcher applied a retrospective chart review design by analysing historical medical records from the level 1 trauma centre at Inkosi Albert Luthuli Central Hospital (IALCH) from January 2017-December 2018. A retrospective study is conducted utilising data on occurrences from the past. Often, the data has already been gathered and entered into a database.

3.3. Study setting

This study took place in Durban, eThekwini district, the largest city in the Kwa-Zulu Natal province and the third largest city in South Africa with a land area of 2556 square kilometres. In 2016, the estimated eThekwini population was 3 702 231, with 64.8% of its population between the ages of 15-64 years (Municipalities of South Africa 2021).

The study was conducted at Inkosi Albert Luthuli Central Hospital, a level I trauma centre (Trauma Society of South Africa accredited), within a quaternary facility equipped to manage all critical patients. The neurosurgery department in IALCH consists of a total of 92 beds: 64 for adults and 18 for paediatric patients. There are two operating theatres, one for elective surgery and the other for 24-hour emergencies

and electives. If no acute neurosurgical care such as invasive monitoring or surgery is required, patients may be transferred to another facility (South Africa, Department of Health 2006:55). The trauma service at IALCH offers eight ICU beds and two High Dependency Unit beds with a dedicated trauma theatre and receiving unit. It is the only unit at IALCH that directly admits patients from the scene and accepts patients as inter-hospital transfers, both polytrauma and major TBI when the neurosurgery unit is over capacity (Cheddie *et al*., 2011). Patients were transferred to IALCH from surrounding provincial hospitals. Figure 1 depicts the positions of provincial hospitals in KwaZulu-Natal.

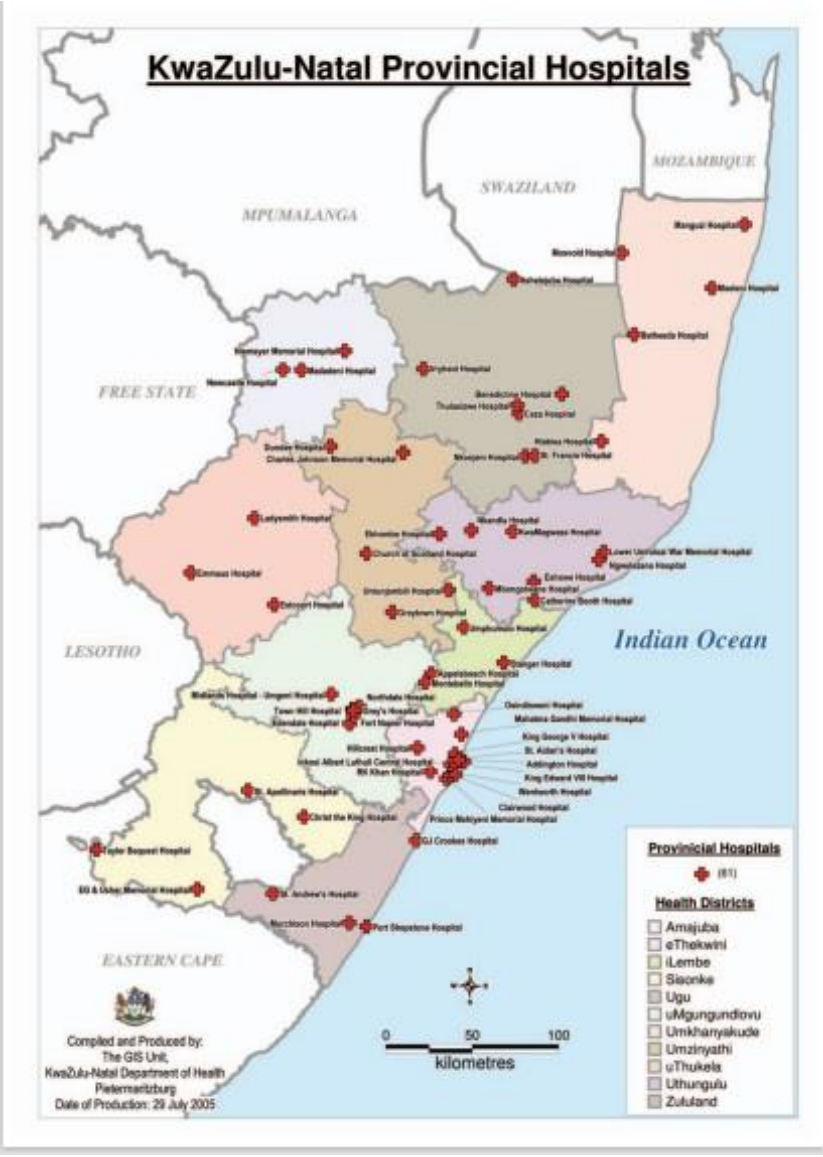

Figure 1: Map of provincial hospitals in KwaZulu Natal (Compiled and produced by: The GIS unit, KwaZulu-Natal, Department of Health. Pietermaritzburg. Date of production: 29 July 2005)

3.4 Study population

The target population for this study involved patients admitted to IALCH and patients who meet the requirements of the inclusion criteria. The target population included patients who were directly admitted to IALCH and patients who were transferred from base hospitals for superior patient management for TBI. Direct admissions refer to patients transported directly to IALCH, either transported privately or by emergency medical services.

3.5 Outcome measure

In this study, a good outcome is referred to as patients who survived severe TBI to discharge despite the method of transportation to a level 1 facility. Unfortunately, the researcher was unable to identify Glasgow Outcome Scale (GOS) at discharge because patients are often transferred back to base hospitals for continued treatment without a GOSE being recorded on the system.

3.6 Aim of the study

The aim of this study was to describe and determine the predictors of outcome in severe traumatic brain injury patients admitted at a level 1 trauma facility.

3.7 Objectives of the study

1. Describe patient outcome following severe traumatic brain injury according to their transport method to a level 1 facility.
2. To determine the relationship between the transport method to hospital and outcomes following severe traumatic brain injury.
3. Describe outcome predictors that predict mortality in severe traumatic brain injury.

3.8 Sampling

The sample should represent the target population as much as possible with minimal error. For the purpose of this study, the population was separated according to their medical diagnosis (severe TBI or no TBI and over the age of 12); therefore, the population included all patients treated in the trauma department of IALCH with a provisional diagnosis of ‘severe traumatic brain injury’. Stata statistical software V15.1 (StataCorp LLC, Texas) was utilised to determine the sample size required to conduct this study. A sample size of 194 patients was required to estimate the proportion of patients with good outcome following severe traumatic brain injury within $\pm$ 10% with a probability of 95%.

3.9 Inclusion criteria

- Patients who sustained a severe traumatic brain injury and older than 12 years of age.
- Patient's initial GCS was within 3-8, or
- when the patients presented with severe abnormalities on CT scan imaging performed in-hospital, namely those requiring neurosurgical intervention or more than 48 hours of intubation and neuroprotective ventilation.

3.10 Exclusion criteria

- Patients who did not sustain a severe traumatic brain injury.
- Paediatrics under 12 years of age.

3.11 Data collection

The data was collected from the IALCH admission registry. All hospital records are electronically recorded, including the initial admission data, daily clinical records, imaging studies, and laboratory results. The quantitative data were collected by means of hospital record analysis. The hospital records of patients who met the inclusion criteria were retrieved from the database covered by the University of KwaZulu-Natal Biomedical Research Ethics Committee (UKZN BREC) class approval for retrospective chart review studies. The researcher completed a short course on the Meditech system, studying the functioning of the database at IALCH. The Meditech system is a computerised electronic patient record system and is utilised to ensure the accuracy and comprehensibility of entries. The hospital records were extracted from the hospital database, processed, and entered onto an Excel Spreadsheet (Microsoft Corp, Redmund WA) to ensure confidentiality. Confidentiality was ensured by ensuring file level protection allowing the researcher to lock down the excel file with the use of a secure password.

3.12 Data analysis

Descriptive data analysis was used to analyse the quantitative data. Descriptive analysis examines past events and aims to describe what has happened. Data aggregation was the first phase of the data analysis. This is the process of retrieving data and entering the data into a database in a summarised format. Data were retrieved from the Meditech system at IALCH and entered onto a Microsoft Excel 2016 spreadsheet in a summarised format (Microsoft Corporation, Redmond, WA). The

second phase was data mining. Data mining involves analysing the retrieved data, searching for any patterns or trends, and, if often demonstrated, using visual representation. Quantitative data analysis included trend analysis and cross-tabulation to form inferences between different data sets in the study. Descriptive statistics, including frequency distribution, graphs and tables, were used in the analysis and interpretation of the data. Frequencies and percentages were used for categorical data. The frequency distribution of numeric data was examined for normality and mean or medians were used as appropriate.

A backward stepwise logistic regression model with a probability of removal set at $p > 0.2$ was then used to adjust for possible confounding. P-values, odds ratios and 95% confidence limits are reported. Stata V15.0 software (StataCorp LLC, Texas) was used for statistical analysis. Means (SD) or medians (IQR) were used for numeric data depending on their frequency distribution. The chi square test or Fisher's exact test was used to determine associations between the categorical variables and the outcome of patients (dead/alive). T-tests or Mann-Whitney were used to compare numeric data. The chi square test was performed to determine any correlation between the method of transportation and length of stay. Factors associated with outcome (dead/alive) were identified using chi square or Mann-Whitney tests in bivariate analysis.

Figure 2: Patient data that was collected

Once the data was obtained, it was categorised into groups, as illustrated in Figure 2, which allowed for easy access to specific patient data as required.

3.13 Validity and reliability of the study

Validity and reliability of the study was ensured by applying internal validity, external validity, reliability, and objectivity. The validity of the quantitative data collection instrument was ensured by conducting a detailed literature review prior to the development of the structured data collection spreadsheet by ensuring that all vital details regarding the study were included in the data collection spreadsheet. The medical records obtained from IALCH were analysed, processed, and entered onto a database using a standardised proforma to ensure comparable data from each included patient. The content validity of the data collection instrument was assessed

by research supervisors who are considered emergency medical care and research experts.

The researcher was thoroughly trained in the use of the Meditech system, ensuring the reliability of the data collection instrument. Reliability was increased by standardising components of the data collection instrument.

3.14 Ethical Considerations

Ethical approval to conduct the study was granted by the Biomedical Research Ethics Committee of the University of Kwa-Zulu Nata (BCA207-09) (Annexure A). No further gatekeeper permissions were required as the researcher accessed the data under the supervision of the principal investigator.

Strict patient confidentiality and anonymity was maintained throughout the research study. No personal information was included in the data collection process to ensure patient anonymity. During the research process, data was captured and stored on a password-protected laptop, only allowing access to the researcher. The data was captured into a Microsoft Excel spreadsheet, which will be destroyed five years after the completion of the study.

3.15 Conclusion

The chapter presented the research design, study population, sampling methods, and data collection used to conduct this research study. Methods of establishing the validity and reliability of the study, such as internal validity, external validity, reliability, and objectivity, were also discussed. The next chapter presents the results of the study.

Chapter 4

Results

4.1 Introduction

The Trauma Service and Trauma Intensive Care Unit at Inkosi Albert Luthuli Central Hospital (IALCH) admitted 566 major trauma cases (adults and children) during the study period. Those with severe TBI on the basis of GCS or CT findings were included in this study. Data for 202 patients who sustained severe traumatic brain injury from January 2017 to December 2018 were obtained. Data from patients under 12 years of age were excluded from this study. The findings from this study involve bivariate and multivariate descriptive statistics and are presented as a descriptive narrative study.

4.2 Demographics

Demographics data from patients included in this study are summarised in Table 4. There were 4.6 times more males than females in the study, while the majority of the participants were 21-35 years of age. Females and patients between 13-20 years of age accounted for the minority of the study. A chi square test for independence was conducted to investigate the relationship between severe TBI and age (p-value 0.11) and sex (p-value 0.7).

Table 4: Demographic variables

Characteristics		**Alive**		**Dead**		**N**
		n	%	n	%	
Sex	Male	122	85.3%	44	74.6%	167
	Female	21	14.7%	15	25.4%	36
Age	13-20 years	20	14.0%	5	8.5%	25
	21-35 years	70	49.0%	25	42.4%	95
	36-49 years	33	23.1%	19	32.2%	52
	>50 years	20	14.0%	10	16.9%	30

4.3 Method of transportation

The majority of participants (84.7%) were transferred to IALCH from other hospitals, while a lower proportion of patients admitted directly to the IALCH trauma department compared to inter-hospital transfers (IHT). As demonstrated in Table 5, patients with direct admission to IALCH had significantly higher mortality (64.5%) than those transferred from other hospitals (22.8%). The results of this study revealed a significant association between the method of transportation and patient outcome ($p<0.001$). A total of n=132 (77.2%) of patients who were transferred from base hospitals survived TBI indicating a good proportion of patients made a good initial recovery after receiving definitive treatment; however, the long-term outcome could not be assessed. Direct admissions had a statistically shorter length of stay (p-0.004) compared to IHTs, proposing an accelerated neurological recovery following direct admissions or a more rapid early death rate.

Table 5: Method of transportation vs patient outcome

	Patient Outcome					**Odds of death**			
	Dead		Alive		Total	OR	95% CI		p-value
Method of Transportation	n	%	n	%	n				
Inter-hospital transfer	39	22,8%	132	77,2%	171	ref	ref	ref	
Direct admission	20	64,5%	11	35,5%	31	6,15	2,72	13,94	<0.001

4.4 Mechanism of injury

Table 6 depicts the mechanism of injury resulting in severe traumatic brain injury in association with mortality. The mechanism of injury that accounted for the majority of injuries were motor vehicle collisions at 41.1%, followed by pedestrian vehicle collisions at 29.7%. Falls and blunt assault accounted for 9.4% and 13.4%, respectively. Other causes of injury, such as ‘found down’ and penetrating assault, accounted for the remaining 6.4%.

Table 6: Mechanism of injury vs mortality

Mechanism of injury	n	%	Mortality (%)
Motor vehicle collision	83	41.1%	32.9%
Pedestrian vehicle collisions	60	29.7%	31.7%
Falls	19	9.4%	21.1%
Blunt assault	27	13.4%	29.6%
Other including 'found down' and penetrating injuries	13	6.4%	7.1%
Total	202	100%	

Motor vehicle collisions accounted for the highest cause of mortality n=27 (32.9%). Of the 59 mortalities (29.2%), a further 19 were due to pedestrian vehicle collisions, accounting for 31.7% of the deaths. Falls and blunt assault accounted for n=4 (21.1%) and n=8 (29.6%), respectively. The minority of n=1 (7.1%) of deaths was caused by 'other' causes. The overall p-value 0.33 shows no significant association between mechanism of injury and mortality.

4.5 Length of stay

Patients who were transported to IALCH directly from the scene had a median hospital length of stay of four days (p=0.0006) compared to inter-hospital transfers, which had a median hospital length of stay of nine days. A significant 54.8% of patients directly admitted to IALCH were admitted for <4 days (p=0.004). For patients transported via inter-hospital transfers, a lower 25.7% of patients were admitted for <4 days. Approximately half of a number of patients (47.5%) who were admitted had an associated LOS between 10 and 94 days. Table 7 represents the relationship between the length of stay and method of transportation.

Table 7: Length of stay vs method of transportation

Length of Stay	Direct Admission		Inter-hospital transfer		Total		p-value
	n	%	n	%	n	%	
0-4 days	17	54,8%	44	25,7%	61	30,2%	0,004
5-9 days	6	19,4%	39	22,8%	45	22,3%	
10-94 days	8	25,8%	88	51,5%	96	47,5%	
Total	31	100,0%	171	100,0%	202	100,0%	

A total of 12 patients did not survive the first 24 hours after admission and were excluded from the following results. A two-sample Wilcoxon rank-sum (Mann-Whitney) test found a statistically significant association between mortality and length of stay (p-value 0.001), but this did not hold for the type of transportation (direct vs transfer). Table 8 depicts the association between the length of stay, method of transportation and mortality.

Table 8: Length of stay vs mortality and method of transportation

	Length of stay				
	n	median	IQR		p
Mortality					
Dead	47	5	3	10	0,001
Alive	143	9	6	15	
Total	190	9	4	13	
Transportation					
Direct admission	22	6	4	10	0,21
Inter hospital	168	9	5	13,5	
Total	190	9	4	13	

Table 9 illustrates the mortality rates of those surviving more than 36 hours, excluding early deaths. Of the total of 59 deaths, 21 (36%) patients died within the first 36 hours. The majority of patients (n=12) who died within the first 36 hours were part of the direct

admission group whilst only n=9 patients who were part of the IHT group died within the first 36 hours.

Table 9: Mortality in patients admitted less than 36 hours

	Alive		Dead		
	n	%	n	%	Total
DA	11	35%	20	65%	31
IHT	132	77%	39	23%	171
Total					202

*DA – Direct admission
*IHT – Inter-hospital transfer

4.6 Vital signs

4.6.1 Pupil response

Pupil responses from 41 patients were categorised as 'unknown' due to the inability to assess the pupils caused by peri-orbital oedema. A total of 81 patients presented abnormal pupil response on arrival at the emergency department at IALCH. The majority of patients with an abnormal pupil response n=62 (67%), survived, while n=31 (33.3%) of the patients died. As indicated in Figure 3, the relationship between pupillary response and mortality was examined. The relationship between these two variables was found to be significant (p=0.28). A lower proportion of patients (33.6%) presented with normal pupillary response with a higher percentage of these patients (37.1%) surviving TBI. A multivariate backward stepwise logistic regression analysis with p=0.3 was performed and did not reveal a significant association between these two variables.

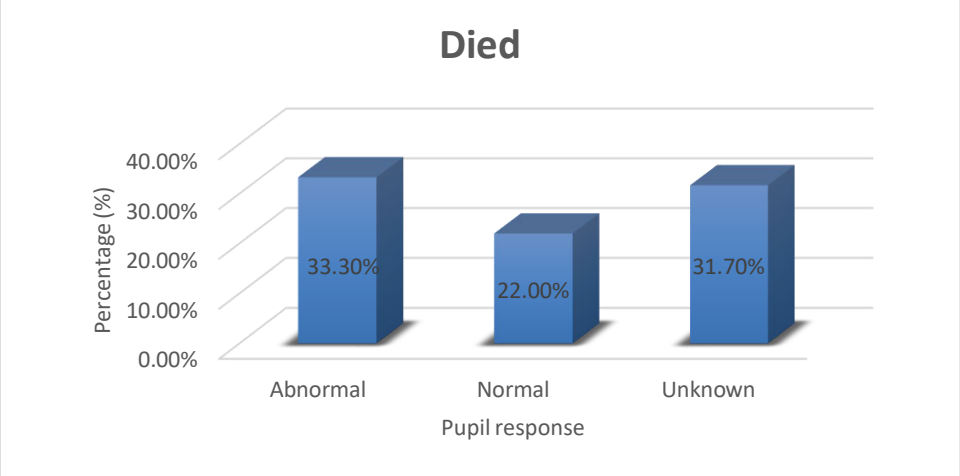

Figure 3: Number of non-survivors according to their initial pupil response

4.6.2 Hypotension

Hypotensive patients were defined as those with a systolic blood pressure < 90mmHg. A majority of 141 patients (72.7%) were not hypotensive on arrival at the ED and survived, while 27.3% of patients who were not hypotensive on arrival at the ED died. Table 10 demonstrates the number and percentage of patients who survived and died according to their blood pressure at the ED. Patients who were hypotensive on arrival at ED had significantly higher mortality compared to patients who were not hypotensive (p-value 0.004).

Table 10: Mortality associated with blood pressure on arrival at the ED

	Alive		**Dead**			**p-value**
BP	n	%	n	%	Total	
<90	2	25.0%	6	75.0%	8	0,004
>=90	141	72.7%	53	27.3%	194	
Total	143	70.8%	59	29.2%	202	

*BP = Blood pressure

In the multivariate analysis, the results did not show any significance between mortality and SBP (p-value = 0.789). Patients who were hypotensive were significantly more likely to be direct admissions (60%) compared to interhospital transfers (12%). Figure 4 demonstrates the relationship between SBP and mortality in the multivariate analysis.

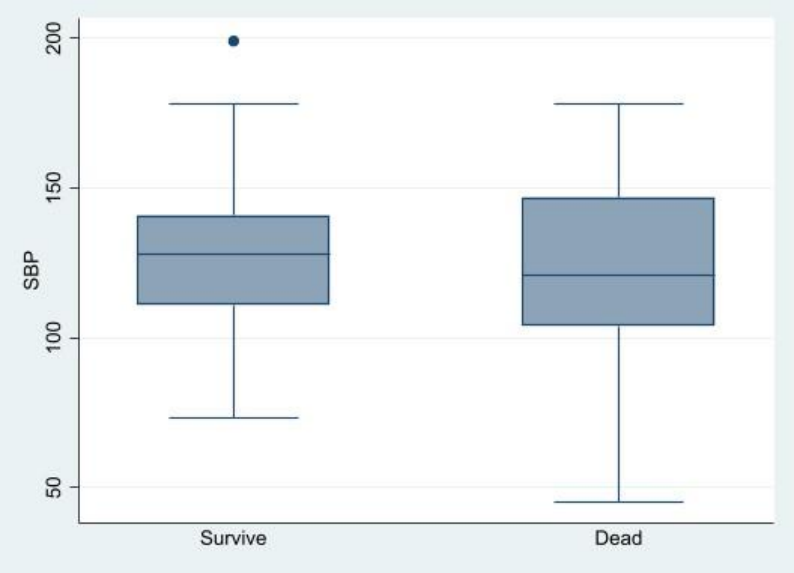

Figure 4: SBP vs mortality

4.6.3 Hyperglycemia

Hyperglycemia was defined as patients with haemoglucose test of (HGT) > 10.0mmol/L. An unsubstantial number of patients (n=30; 14.9%) arrived at the ED with hyperglycemia during the study period. Thirteen of these hyperglycemic patients had a fatal outcome, demonstrating a trend towards significance (p-value=0.07) that may be affected by sample size. The majority of patients included in this study n=134 (72.4%), were not hyperglycemic and survived. Table 11 represents the association between hyperglycemia and survival.

Table 11: Mortality associated with hyperglycemia on arrival at the ED

HGT	**Alive**		**Dead**			
	n	%	n	%	Total	p-value
>10.0mmol/L	13	43,3%	17	56,7%	30	0,07
<10.0mmol/L	46	26,7%	126	73,3%	172	
Total	59	29,2%	143	70,8%	202	

*HGT = Haemoglucose test

4.6.4 Hypoxia

Hypoxia occurs in patients with SpO2<90%. As represented in table 12, seventeen patients were hypoxic on arrival at the ED. Of these 17 patients, n=8 (47.1%) were non-survivors, and n=9 (52.9%) of patients survived. There was no significant association between hypoxia (SpO2<90%) and mortality (p=0.33).

Table 12: Mortality associated with hypoxia on arrival at the ED

	Alive		**Dead**			**p-value**
SpO2	n	%	n	%	Total	
SpO2<90%	8	47,1%	9	52,9%	17	0,33
SpO2>90%	51	27,6%	134	72,4%	185	
Total	59	29,2%	143	70,8%	202	

*SpO2 = Peripheral capillary oxygen saturation

4.7 Physiological Scoring System

4.7.1 Glasgow Coma Scale

A significant correlation exists between GCS 13-15 and survivors (p=0.005). All patients who arrived at the ED with GCS 13-15 survived hospital admission, despite the fact that severe TBI was identified on the CT scan. The majority of patients (55.9%) with an initial GCS 6-12 survived, while n=27 (45.8%) of patients in this GCS group did not survive. A total of 32 (54.2%) patients with an initial GCS 3-5 died. Figure 5 depicts the mortality rate associated with GCS.

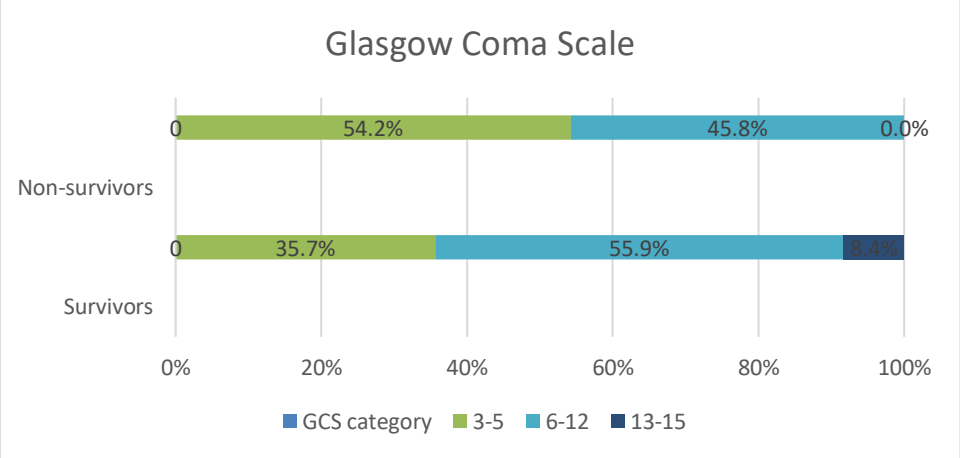

Figure 5: Mortality rate associated with GCS

The Kruskal Wallis test was applied to the results revealing a significant association between the median length of stay and GCS category (p-value = 0.001), as depicted in Table 13.

Table 13: GCS associated with LOS

	Length of stay				
GCS	n	median	IQR		p
3-5	83	6	3	12	0,001
6-12	107	9	5	15	
13-15	12	3,5	3	7,5	
Total	202	8	4	13	

*GCS = Glasgow coma scale

4.7.2 Revised trauma score

There was a statistically significant (p=0.03) difference between the revised trauma score (RTS) in survivors and non-survivors included in the study. The majority of patients (61.5%) included in this study with RTS 6-8 survived severe traumatic brain injury. Of those with RTS <+5, 54.5% did not survive. Table 14 depicts the RTS statistical values. The mean RTS value for the total sample was 5.4 ± 1.3. Table 15 depicts the survival probability related to the RTS values.

Table 14: RTS statistical values

Outcome	n	mean	p-value	median	IQR		p-value
Dead	55	5,1±1,2	0,02	5,0	4,0	6	0,03
Alive	135	5,6±1,3		6,0	4,0	6	
Total	190	5,4±1,3		6,0	4,0	6	

Mean±standard deviation

Table 15: RTS vs mortality

RTS	**Alive**		**Dead**		**Total**	**p-value**
	n	%	n	%		
3	2	1.4%	1	1.7%	3	0.03
4	37	25.9%	24	40.7%	61	
5	13	9.1%	5	8.5%	18	
6	58	40.6%	18	30.5%	76	
7	14	9.8%	6	10.2%	20	
8	11	7.7%	1	1.7%	12	
Unknown	8	5.6%	4	6.8%	12	
Total	143	100%	59	100%	202	

* RTS = Revised trauma score

4.7.3 New injury severity score

The new injury severity score (NISS) was categorised into three categories: Mild, moderate and severe. The ‘mild’ category included patients with NISS 1-15, and the moderate and severe categories included patients with NISS 16-49 and 50-75, respectively. In the cohort admitted to IALCH, the median score of NISS was 57.0 for non-survivors and 41.0 for survivors. The two-sample Wilcoxon rank-sum (Mann-

Whitney) test revealed a significantly higher NISS in patients who were non-survivors (p-value < 0.001). This is depicted in Table 16. A Pearson chi^2 test was performed to compare the NISS of direct admissions who survived >= 3 days to all inter-hospital transfers. This test revealed a Pearson chi(1) = 0.7653 and Pr =0.382. A total of ten direct admissions survived >= 3 days in the hospital. Of these ten direct admissions, five (50%) patients had a good/moderate (1-49) NISS, and the other five (50%) had a severe (50-75) NISS.

Table 16: Mortality associated with NISS

NISS	**Alive**		**Dead**		**Total**	**p-value**
	n	%	n	%	n	
Mild (1-15)	1	100,0%	0	0,0%	1	<0.001
Moderate 16-49)	96	81,4%	22	18,6%	118	
Severe (50-75)	46	56,8%	35	43,2%	81	
Total	143	71,5%	57	28,5%	200	

*NISS = New injury severity score

4.8 Complications

A total of n=154 (76.2%) patients did not develop any complications such as ventilator-associated pneumonia, or aspiration, or the need for re-neuroprotection, re-operation, and re-scan during their admission. Forty-two (20.8%) patients developed one complication during admission, while six (3.0%) patients developed two or more complications.

4.8.1 Ventilator-associated pneumonia

The most common complication that patients developed was ventilator-associated pneumonia (10.9%). Of these patients, four (18.2%) were non-survivors. A two-sample Wilcoxon rank-sum (Mann-Whitney) test found a significant association between length of stay and ventilator-associated pneumonia (p-value 0.0005). The median VAP length of stay was 12.5 days (inter-quartile range [IQR] = 9-17 days), whilst the median value for patients who did not develop ventilator-associated pneumonia during admission was 7.5 days (IQR = 4-12 days).

4.8.2 Aspiration

Of a total 202 patients, 16 patients encountered aspiration as a complication. The majority of patients n=186 were not associated with aspiration. The median aspiration length of stay was six days (IQR 6-13.5). There were no significant findings (p=0.32) associated with aspiration.

4.8.3 Re-operation

The majority of patients n=198 did not require re-operation during admission. The median re-operation length of stay was six days (IQR 4-11 days). There were no significant findings (p=0.71) associated with re-operation.

4.8.4 Re-scan

The minority of patients n=12 required a re-scan during admission in IALCH with a median of 7.5 days. There were no significant findings associated with the re-scan (p=0.79). The findings demonstrated that the median length of stay was 7.5 days, with the IQR 4-12.5 days. Table 17 depicts the number of patients that developed complications during admission to the hospital with the respective median.

Table 17: LOS associated with complications

Complication	n	Median
Ventilator-associated pneumonia (VAP)	22	12,5
Re-operation	4	6
Aspiration	16	9
Re-scan	12	7,5
Total:	54	

4.9 Glasgow Outcome Scale Extended (GOSE)

Despite the intention to record the GOSE as part of this study, it was impossible to determine a GOS of patients at discharge because the majority of patients were transferred back to base hospitals prior to final discharge from the hospital. The researcher was ethically cleared to access patient records at IALCH and not surrounding base hospitals. It was, therefore, impractical to determine GOSE, which aims to show late outcome status and not that at discharge from the hospital.

4.10 Multivariate analysis

Prognostic values of multiple prognostic variables on admission post-severe TBI were studied using both bivariate and multivariate analysis. Multivariate analysis of variance was conducted on numerous variables, including specific vital signs, mechanism of injury, method of transportation, complications, length of stay, and physiological and anatomical scoring systems. After obtaining a strong correlation between direct admission and mortality, the researcher conducted a multivariate model analysis to identify further supporting evidence. A backward stepwise logistic regression with $p < 0.2$ was used to select the variables included in the analysis. Several variables, including GCS, RTS, mechanism of injury, pupil response, hypoxia, hyperglycemia, CT abnormalities and complications, were excluded from the multivariate model as these variables were insignificant with p-values > 0.2.

Consistent with the results from the Mann-Whitney test, the method of transportation appears to have a consistently strong correlation with mortality. Patients transported to the hospital directly from the scene have a higher chance of mortality. Table 18 depicts the results from the bivariate and multivariate analysis associated with the method of transportation.

Table 18: Bivariate and multivariate model analysis between the method of transportation and mortality

Mortality								
	Bivariate analysis				Multivariate analysis			
Transportation	p-value	OR	95% CI		p-value	OR	95% CI	
IHT	ref	ref						
DA	<0.001	6,15	2,72	13,94	0,011	3.52	1,33	9.32

*IHT – Inter-hospital transfer

*DA – Direct admission

A further sensitivity analysis of physiological scoring systems was performed on the data retrieved from the study. GCS was collapsed into two groups in the bivariate model: 3-5 and 6-15. In the initial GCS group 13-15, there were no associated deaths. Logistic regression dislikes ‘0’ cells and consequently merged GCS into two groups. However, GCS was not included in the multivariate model due to insignificant results

obtained in the bivariate model. GCS and RTS disclosed insubstantial p-values in the bivariate model with p=0.5 and p=0.3 subsequently. NISS revealed significant results in the bivariate model with p<0.001, odds ratio of 3.35 and 95% Cl between 1.77 and 6.35, indicating NISS as the best predictor of mortality. NISS was thereafter included in the multivariate model, as seen in Table 19. Consistent with the other results in this study, NISS appears to be the strongest predictor of mortality when compared with other physiological scoring systems (GCS, RTS).

Table 19: Bivariate and multivariate model analysis between physiological scoring systems and mortality

Odds of death (mortality)								
Bivariate analysis					Multivariate analysis			
	p-value	OR	95% Cl		p-value	OR	95% Cl	
GCS								
3-5								
6-15	0,016	0,47	0,25	0,87	0,333	0,53	0,15	1,92
RTS								
<=5								
6-8	0,04	0,52	0,28	0,98	0,462	1,64	0,44	6,14
NISS								
Good/mod (1-49)								
Severe (50-75	<0.001	3,35	1,77	6,35	0,001	3,57	1,65	7,71

In accordance with this study's previous results, early mortality remains a significant variable in determining the length of stay. The length of stay had a significant p-value in the bivariate study and was, therefore, included in the multivariate model, as shown in Table 20, adjusting for possible confounding results. We identified that both groups

of the length of stay, i.e., 5-9 and 10-94, were associated with decreased mortality. Although, there was more variation in the estimate for group 5-9 (95% Cl = 0.05-0.40) than for group 10-94 (95% Cl 0.08-0.41). Both groups had a significant p-value (p-0.001).

Table 20: Bivariate and multivariate model analysis between LOS and mortality

Mortality								
	Bivariate analysis				Multivariate analysis			
	p-value	OR	95% CI		p-value	OR	95% CI	
Length of Stay								
0-4 days	ref	ref	ref	ref				
5-9 days	<0.001	0,15	0,06	0,38	<0.001	0,14	0,05	0,40
10-94 days	<0.001	0,18	0,09	0,38	<0.001	0,18	0,08	0,41

4.11 Conclusion

This chapter presented the results of the study in accordance with the research aims and objectives. The findings of this study revealed that the majority of the patients were young males. It emerged that most patients were involved in motor vehicle collisions when they sustained a severe traumatic brain injury. Furthermore, patients transported directly to the level 1 facility were admitted for a shorter length of stay compared to inter-hospital transfers. Chi square and Mann-Whitney tests were used to identifying factors associated with the outcome. A backward stepwise logistic regression model was used on the association between the prognostic factors and mortality. NISS was found to be the best predictor of mortality, and direct admission was also associated with a shorter length of stay and increased mortality. Variables with insignificant results were not included in the multivariate model. Only specific outcome predictors such as pupil response, hypotension, and Glasgow Coma Scale (GCS) revealed a statistically significant association with mortality rate. Chapter 5 discusses the results of this study.

Chapter 5

Discussion

5.1 Introduction

This chapter discusses the results that were presented in Chapter 4. Chapter 5 compares the results from this study with the findings from existing literature to achieve a more extensive understanding of the results. This chapter aims to address the research objectives outlined in Chapter 1. The research objectives of this study include the following: describe patient outcome following severe traumatic brain injury according to their transport method to a level 1 facility; determine the relationship between the transport method to hospital and outcomes following severe traumatic brain injury and describe outcome predictors that predict mortality in severe traumatic brain injury. As indicated earlier, 565 patients were admitted to Inkosi Albert Luthuli Central Hospital (IALCH) between January 2017 and December 2018. However, only 202 patients met the inclusion criteria and were included in this study.

5.2 Demographics

Traumatic brain injury is the leading cause of increased mortality and morbidity globally (Dewan *et al*., 2018). The main cause of traumatic brain injury in South Africa includes motor vehicle collisions and interpersonal violence (Kong *et al*., 2017). A similar study suggested that transport-related injuries more frequently occur in young males influenced by drugs and alcohol (Hardcastle *et al*., 2016). Likewise, a South African study that investigated 'direct admission versus interhospital transfers to a level 1 trauma unit', also found that males dominated all groups of injuries (Cheddie *et al*., 2011). The proportion of males in the study group was significantly greater compared to females (almost 4:1). Similarly, in the present study, the results revealed that the majority of the patients were males (85.3%) and suffered severe traumatic brain injury whilst only 36 of the 202 patients were female.

The majority of studies suggest sex is not a good predictor of patient outcome (Oremakinde *et al*., 2019). A study by Gupte and colleagues discusses various factors that may influence outcome according to sex. The first factor is the mechanism of injury. Females are more likely to sustain injury from assault or violence. Secondly, male and female brains react differently to the result of an injury on a cellular or molecular level. Thirdly, the repair and recovery process of the brain is different in

males and females. Finally, patterns of extracerebral injury and post-injury complications might be specific to a particular sex (Gupte *et al*., 2019).

Age is one of the most commonly used predictors of patient outcome in TBI and was a more reliable predictor than functional outcome in an earlier study (Oremakinde *et al*., 2019). The results of this study revealed a large portion (47%) of patients involved in trauma-related injuries that resulted in severe TBI were patients between the ages 21 and 35. A total of 70 patients (49.0%) between the ages of 21-35 survived severe traumatic brain injury and were discharged to a lower-level facility for further observation. Amongst all the age groups specified, the mortality rate was the highest in patients 21-35 years, where 25 patients succumbed to their injuries in-hospital (42.4%); however, several of these injuries were severe on arrival at the hospital, and they died during an examination or shortly after arrival at the emergency department. The age group most affected by mortality was 21-35 years of age, making up 42.4% of patients. In contrast, patients between 50-93 years of age accounted for 16.9%. While the younger age group had a higher mortality rate compared to their older counterparts. It would be incorrect to presume an increased risk of vulnerability in the younger population due to the high mortality, as elderly patients are less likely to be involved in high-energy traumatic injuries. This may be attributed to individual behavioural decisions, such as reckless driving, neglecting to use a safety belt, and alcohol intoxication (Dunne *et al*., 2020).

5.3 Mechanism of injury

The most common mechanism of injury in this study was motor vehicle collisions (MVC), accounting for 40.6% of injuries. The category ‘other’ injury under mechanism of injury includes penetrating injuries such as stabbings, gunshot wounds (GSW), and ‘found down’. Motor-vehicle related injuries are the major cause of severe traumatic brain injury globally (Dunne *et al*., 2020). In LMIC, this may be attributed to the shortfall of road safety awareness and education and the development of cities. Despite the fact that violence and industrial accidents are responsible for a large amount of TBIs internationally, road traffic collisions account for approximately 60% of TBI burden (Dunne *et al*., 2020). The World Health Organization speculates that MVCs will become the seventh leading cause of mortality by the year 2030 (Dunne *et al*., 2020). Although high-income countries constitute 46% of registered vehicles around the world, they account for only 10% of MVCs (Dunne *et al*., 2020). In high-income

countries, traffic safety laws and preventative systems have been implemented to reduce TBI resulting from MVCs (Maas *et al*., 2008).

5.4 Method of transportation

Mortality rates are a crucial indication of patient management in critically injured trauma patients (Cheddie *et al*., 2011). The results of this study revealed that 84.7% of patients with severe traumatic brain injury were transferred to IALCH from surrounding hospitals, while only 15.3% of patients were direct admissions. Direct admissions include patients transported directly from scene to hospital after consultation with pre-hospital care providers. Considering that a study indicated decreased mortality in patients directly admitted to a dedicated trauma unit (Cheddie *et al*., 2011). Conversely, this study found a significant increase in mortality in patients directly admitted to the trauma unit. The higher mortality in the direct admission patient cohort may be related to the severity of injury in those admitted directly from the scene. Furthermore, patients who have been transferred to IALCH have been resuscitated and stabilised at the base hospital, arguably with better resources available than in the prehospital setting. In addition, patients who have demised at base hospitals from severe TBI are not transferred to IALCH, thus potentially skewing the results on the actual outcome.

The results of this study revealed a significantly shorter length of stay in direct admissions compared to inter-hospital transfers. A reduction in the length of stay in patients promotes faster discharge from hospitals, reducing the resources used to treat patients and ultimately decreasing the burden on developing communities. However, this data may be skewed by the early deaths in the direct admission cohort. The strong association between the method of transportation and patient outcome is further supported by the bivariate and multivariate analysis in this study, as discussed in 5.9. In accordance with our results from the chi square test, the multivariate analysis revealed method of transportation was proven to be a reliable predictor of mortality. Direct admission has been associated with the poor patient outcome when compared with inter-hospital transfers. Keeping this in mind, critically unstable patients with severe TBI who are transported to the closest hospital will require stabilization prior to transfer and may deteriorate prior to transfer resulting in decreased overall mortality.

5.5 Patient outcome and outcome analysis

Often, healthcare personnel use outcome predictors to assist in clinical triage, resource allocation, decision making and family counselling (Oremakinde *et al*., 2019).

5.5.1 Hypotension, hypoxia and hyperglycemia

Using an SBP of lower than 90mmHg to define hypotension, the data revealed a significant association between hypotension and mortality. The majority (72.7%) of patients were either normotensive or hypertensive on arrival at IALCH. This may be due to the strong association between the method of transportation and hypotension. Notably, the majority (60%) of patients who were hypotensive on arrival at the ED were transported directly from the scene. Therefore, in the multivariate model, transportation is the independent factor, and SBP is not independently associated with death. This may be because patients were stabilised at the base hospitals prior to transfer, thereby treating the initial hypotension. While the pre-hospital healthcare personnel-initiated treatment prior to transportation to the hospital on direct admissions in an attempt to prevent secondary injury, the hypotension may have been incompletely reversed with resulting mortality and may also be affected due to the small sample size of the hypotension cohort (n=8)

Kulesza *et al*. (2015) proposed that hypotension and hypoxia post-TBI is identified as crucial secondary injury related to an unfavourable outcome. This statement is consistent with the results of this study, which revealed a significantly higher mortality rate in hypotensive patients compared to patients who were normotensive. This finding is not altogether surprising as retrospective studies performed on wide databases such as the Traumatic Coma Data Bank and the National Paediatric Trauma Registry proposed that hypotension post-TBI doubles the mortality rate (Manley *et al*., 2001). A link between systemic hypotension and poor patient outcome has been described in retrospective studies (Manley *et al*., 2001). Injury to the brain causes the brain to become prone to secondary ischemic injuries. This may be aggravated by the inability to improve cerebral blood flow.

Hypotension, hypoxemia and acute anaemia results in the inability to improve cerebral blood flow (CBF) (Manley *et al*., 2001). A study performed by Manley and colleagues found up to 90% of patients post-autopsy had a remarkably decreased CBF after injury to the brain (Manley *et al*., 2001). They (Manley *et al*., 2001) also stated that patients

who experienced one or more hypotensive events, despite oxygen saturation levels, had a significantly increased morbidity and double the mortality (Manley *et al*., 2001). Studies also revealed a decreased rate of survival in other trauma patients in patients who are hypotensive or hypertensive (Bhandarkar *et al*., 2017). A study performed by Bhandarkar *et al*. suggested a SBP=110mmHg is related to reduced survival and a decrease of 10mmHg in SBP increases the probability of mortality by 4.8% (Bhandarkar *et al*., 2017). Furthermore, a study performed by Newfield *et al*. determined a significant increase in mortality from 45% to 83% in patients with shock (SBP<90mmHg) within the first 24 hours (Manley *et al*., 2001).

Using SpO2 < 92% to define hypoxia, the results of this study did not identify any significant association between mortality and hypoxia. Keeping in mind patients received initial medical care at the lower-level facility and in the pre-hospital environment, possibly correcting and preventing hypoxic events prior to transportation to IALCH. Another reason for the aforementioned finding is possibly because the majority of the patients (80.2%) were intubated prior to transportation to IALCH and were not hypoxic on arrival at the ED. Hypoxia was measured using pulse oximetry instead of arterial blood gas. Therefore, it is a possibility that one or more hypoxic events were undetected. In conjunction with the results of this study, a review conducted by Rubenson Wahlin *et al.* (2018) did not identify any significant association between pre-hospital hypoxia and poor patient outcome. As suggested by Moppett *et al.* (2007), several observational studies reported a relationship between early hypoxia and poor outcome, with hypoxia defined as SpO2<90% or a partial oxygen pressure <60mmHg. Conversely, a study performed by Manley *et al.* (2001) did not reveal any significant relation between hypoxia and mortality.

Kulesza *et al*. (2015) state that hyperglycemia is a source of secondary brain injury post-TBI and is related to a worse outcome. In the current study in KZN, approximately 15% of patients presented with blood glucose level > 9.0mmol/L. Further analysis of the results of this study revealed a trend toward significance between hyperglycemia and mortality, suggesting that further research on mortality associated with hyperglycemia would be worthwhile with a larger cohort. Similarly, previous research indicated that patients with poor outcome presented with higher blood glucose levels compared to patients with good outcome (12.1mmol/L^{-1} vs 9.3mmol/L^{-1}) (Moppett, 2007). A study conducted by Rau *et al.* (2017) identified a marked increase in serum

glucose levels in patients with severe TBI compared to mild TBI. In TBI, any response to stress may result in stress-induced hyperglycemia contributing to tissue lactic acidosis in the brain leading to neuronal injury (Rau *et al*., 2017). Hyperglycemia is often recognised after TBI and is associated with worse patient outcome for both mortality and functional recovery in adults and children (Moppett, 2007). Various studies have revealed an association between increased mortality and morbidity and an increase in stress-induced hyperglycemia in trauma-injured patients (Rau *et al*., 2017).

5.5.2 Pupil response

Pupil response, age and motor score were significant variables in predicting mortality (Oremakinde *et al*., 2019). GCS and pupil response provide healthcare professionals with predictive details about the head-injury patient (Brennan *et al*., 2018). Poor pupil response is associated with worsened patient outcome (Brennan *et al*., 2018). A study by Brennan *et al*. (2018) revealed an association between worsened patient outcome and pupil response declines. Unlike GCS, there is minimal change in pupil response across pupil evaluation, making pupil response a strong prognostic component. Pupil response is also a more unbiased factor of a patient's condition because it is unlikely to be influenced by poor patient cooperation (Majdan *et al*., 2017). A South African study also found a relationship between pupillary findings and patient outcome (Sobuwa *et al*., 2014).

Brain injury and herniation may compress the third cranial nerve resulting in fixed and dilated pupils (Sobuwa *et al*., 2014). Central transtentorial herniation may lead to bilaterally fixed and dilated pupils, whereas lateral transtentorial herniation may lead to ipsilateral fixed and dilated pupillary findings (Sobuwa *et al*., 2014). Fixed and dilated pupils are strongly related to mortality (Sobuwa *et al*., 2014). The results of this study revealed a significant association between pupil response and mortality. The majority of patients with severe TBI were categorised with 'abnormal' pupillary response suggesting an association between pupil response and TBI. Of patients who presented abnormal pupillary response (n=93), 33% did not survive injuries suggesting an association between pupil response and mortality. Several patients (n=41) had 'unknown' pupillary response, which may be due to the inability to assess pupils, such as peri-orbital oedema caused by facial injuries.

5.5.3 NISS

The new injury severity score (NISS) is the sum of the three most severe injuries and is a better predictor of mortality than the injury severity score (Stevenson *et al*., 2001). The three highest Abbreviated injury scale (AIS) was used to calculate the NISS. The NISS was divided into three categories: Mild (NISS 1-15), moderate (NISS 16-49), and severe (NISS 50-75). This study showed a significant association between NISS and mortality. Non-survivors had a significantly higher mean and median NISS than survivors who were discharged.

A recent study performed by Li and Ma (2021) found that NISS and ISS are comparatively high predictors of mortality. Although, results advise NISS as a more accurate predictor of mortality in severe trauma (Li and Ma, 2021). Additionally, NISS has exhibited evident precedence in predicting ICU length of stay and admission (Li and Ma, 2021).

The multivariate analysis showed that NISS could be used as an independent predictor of mortality. In fact, NISS was the strongest predictor of mortality in the multivariate analysis in this study, although GCS and RTS were also proven to be reliable predictors of mortality (p=0.02). Likewise, Meena and Mehta (2019), found NISS to be a superior outcome predictor compared to RTS, a physiological scoring system (Meena and Mehta, 2019). Further results of this current study revealed that half of the direct admissions who survived >= 3 days had a good or moderate NISS, and the remaining half had a poor NISS. This suggests that some patients with a poor NISS who were transported directly to a level 1 facility survived despite the poor prognosis. This may be due to efficient, appropriate clinical management of severe TBI with specialised equipment.

5.5.4 GCS

The Glasgow Coma Scale (GCS) objectively expresses the degree of decreased consciousness in acute medical and trauma patients (Jain and Iverson, 2018). The scale evaluates a patient's level of consciousness on the report of three aspects of responsiveness: eye opening, motor and verbal responses (Jain and Iverson, 2018). Outlining these aspects provides a concise communicable representation of a patient. GCS is utilised in over 75 countries and is an important constituent of the National

Institutes of Health (NIH) Common Data Elements for studies of head injury and the International Classification of Diseases (ICD) 11 revision (Jain and Iverson, 2018).

According to previous studies, GCS has a linear correlation with mortality (Kulesza *et al*., 2015). A decreased GCS on admission is associated with poor outcome. A study performed by Sobuwa and colleagues (2014) found that a higher GCS is associated with better patient outcome. The results of this study corresponded with Sobuwa and colleagues. GCS was assessed on arrival at the emergency department (ED). However, several patients were already intubated on arrival at ED by either the doctors at base hospitals or by paramedics in the pre-hospital environment, in which case the patients presented with a lower GCS on arrival at IALCH ED. This study found a significant association between GCS and mortality. The majority of patients (n=107) presented with a GCS 6-12 with a 45.8% mortality. For patients with the lowest GCS scores (3-5), there was an associated mortality rate of 54.2%. There were no deaths amongst patients who arrived with an initial GCS 13-15, suggesting poor outcome in patients with a lower GCS. A study performed by Perel *et al*., revealed that the majority (50%) of predictors used was GCS in the 53 prognostic models he evaluated. Perel *et al*. also suggested that GCS has been an extensively utilised tool by some of the most prevalent prognostic models in high-income countries (Perel *et al*., 2006).

5.5.5 RTS

Revised trauma score (RTS) is regarded as one of the easiest triage tools utilised in the emergency department (ED) and is often used in the pre-hospital environment (Manoochehry *et al*., 2019). RTS incorporates the Glasgow Coma Scale (GCS), respiratory rate (RR) and systolic blood pressure (SBP) to determine a score predicting patient outcome. The RTS was calculated using the formula RTS+0.9368 x GCS + 0.7326 x SBP + 0.2908 x RR to determine a revised trauma score value between 0 to 8, allowing fractions. In this study, RTS values were rounded off to the nearest whole number and divided into two categories: RTS <=5 and RTS 6-8. Mortality is significantly higher in patients with RTS <=5 compared to RTS 6-8. The mean and median RTS is significantly lower in non-survivors compared to survivors. The results of this study were in line with the results of a similar study performed by Manoochehry and colleagues (2019), suggesting a high level of accuracy between RTS and determining patient outcome.

A fundamental observation was the fact that the predictors GCS and RTS who passed the bivariate analysis with significant p-values, were not subsequently included in the multivariate model with the other variables. The reason is that in the multivariate model, GCS and RTS were no longer significant with p=0.5; OR-0.8 and p=0.3, respectively. GCS and RTS had very little impact once adjusted for the other variables in the multivariate model. This may suggest that GCS and RTS are only significant in the bivariate analysis because of its associations with other predictors.

5.6 Length of stay

The length of stay was determined by calculating the total amount of days that the patient was admitted to the hospital before being discharged to a step-down facility, as no patients are directly discharged home from IALCH. The results of this study revealed a significant association between the median LOS and GCS category suggesting that patients with a lower GCS were admitted to hospital for longer than patients with a higher GCS.

A comparison was performed between direct admission patients with LOS >= 3 days and inter-hospital transfers. A total of 20 direct admission patients died during admission at the hospital, whilst 12 of these patients died within the first three days. A lower proportion of deaths were identified in the IHT group, with nine patients dying within the first three days. These deaths usually occur as a result of severe or non-survivable injuries. Patients may also be transported to the emergency department and classified as 'dead on arrival'. Late deaths often result from multiple organ failure and sepsis. Patients also sustained irreversible head injuries, and medical treatment was withdrawn, allowing natural death.

Often, mechanical ventilation is required shortly after the initial traumatic brain injury to maintain the airway and promote adequate gaseous exchange (Silva *et al*., 2018). Glasgow Coma Scale < 9 is an indication of endotracheal intubation and mechanical ventilation (Silva *et al*., 2018). Patients who are ventilated for more than 48-72 hours are at risk of developing ventilator-associated pneumonia, affecting the lung parenchyma (Silva *et al*., 2018). This is consistent with the results of this study, which found a significant association between the length of stay and ventilator-associated pneumonia (VAP), suggesting that patients who developed VAP are admitted to the

hospital for a longer period of time. There are other factors that may influence the length of stay that were not included in this study, such as extracranial complications.

5.7 CT scan

Traumatic brain injury is based on clinical symptoms such as loss of consciousness and retrograde or anterograde amnesia (Maas *et al*., 2008). Additional factors to consider include mechanism of injury (MOI), risk factors and the patient's level of consciousness. (Maas *et al*., 2008). CT scan is used to identify structural injuries and intracranial hematomas. Traumatic intracranial injuries often occur in moderate-severe injuries but may also occur in patients presenting with GCS 14 (Maas *et al*., 2008). The possibility of intracranial injuries is rare in patients with GCS 15 unless risk factors are present. Guidelines recommend a CT scan in all patients with GCS<14 and GCS 15 with risk factors such as vomiting, age, MOI, neurological deficit, duration of amnesia, and anticoagulation medications (Maas *et al*., 2008).

Specific CT scan abnormalities, including EDH, SDH, ICH, ventricular effacement, basal cistern effacement, IVH, SAH and midline shift, have been shown to be reliable outcome predictors in head injury (Oremakinde *et al*., 2019). Studies suggest that these abnormalities are more reliable outcome predictors than the Marshall classification (Oremakinde *et al*., 2019). In this study, CT scan abnormalities were grouped in two: >2 abnormalities and <2 abnormalities. Contrary to other studies that suggest CT scan findings are crucial clinical predictors, the results of this bivariate study did not yield any significant results. Regardless of the number of abnormalities noted on the CT scan, the results were insignificant (p=0.59), and CT scan findings were not included in the multivariate analysis. This may be due to the rapid recognition and definitive management administered by neurosurgeons at the level 1 trauma facility.

5.8 Complications

Unexpectedly, 76.2% of patients did not suffer from complications such as VAP, aspiration, or the need for re-operation, re-scan, and re-neuroprotection during admission. The data from this study demonstrated that the majority of patients (n=162 (80%)) were intubated either prior to inter-hospital transfer by paramedics or on arrival at the emergency department. The results of this study suggest that 31% of intubated patients died, which can be explained by the severity of the injuries sustained, and the

need for emergency advanced airway management. A study performed by (Li and Ma, 2021) revealed that VAP occurred in a minority of patients in their meta-analysis. Similarly, the results of this study revealed only 22(11%) of 202 patients developed VAP. It was also demonstrated that aspiration was the second most common cause of complications in severe TBI, with a 31.3% mortality rate. Re-operation, re-scan and re-neuroprotection were only associated with 4,12, and 0 patients, respectively. Despite these findings, this study did not disclose a significant association between complications and mortality, with an insignificant p=0.9 in the multivariate model.

5.9 Conclusion

This study highlights the need for a prospective study on outcome predictors and mortality related to transportation methods in patients with severe traumatic brain injury. This study determined that direct admissions had a remarkably reduced length of stay, which may be skewed by early deaths. The results of this study can inform future practice in terms of the decision-making of pre-hospital healthcare workers.

The study confirms a higher mortality associated with traumatic brain injury in younger males. Since the main mechanism of injury of traumatic brain injury are motor-vehicle collisions and pedestrian-vehicle collisions, increased awareness of road safety is suggested to reduce the incidence of traumatic injuries. This study also identified hypotension as a major contributing factor to mortality in severe TBI, suggesting that the rapid prevention and management of hypotension in the pre-hospital environment is crucial.

A relevant association between RTS, NISS, GCS and mortality was noted. However, NISS had a greater statistical correlation with mortality when compared to RTS and GCS.

Chapter 6

Summary, recommendations, limitations, and conclusion

6.1 Introduction

Limited studies exist related to outcome and outcome predictors of severe TBI in South Africa. This study contributed by expanding existing knowledge of severe TBI in the South African context. Three objectives were identified in order to achieve the research aim of describing and predicting outcome at hospital discharge in patients with severe TBI at a level 1 trauma unit. This chapter summarises the findings of the study, introduces recommendations to increase awareness regarding severe TBI and makes suggestions for future research topics. It discusses the limitations of the study; and provides a conclusion of the study. Due to the inability to obtain data for one of the objectives, this resulted in three overall objectives.

6.2 Summary

6.2.1 Patient outcome according to the method of transportation to a level 1 facility

The first research objective was to describe patient outcome following severe TBI according to their transport method to a level 1 facility. In this study, a good outcome is referred to patients who survived severe traumatic brain injury despite the method of transportation to a level 1 facility. The study revealed that a large percentage (64.5%) of direct admissions who were included in this study did not survive. Mortality is significantly greater in direct admissions compared to inter-hospital transfers. However, the study found a significantly shorter length of stay in direct admissions when compared to inter-hospital transfers. As mentioned, the majority of patients were transferred to IALCH from surrounding hospitals. The majority of the patients who survived were inter-hospital transfers (77.2%), while 35.5% of patients who survived were direct admissions. This indicated a good proportion of patients presented with good outcome post-severe TBI when they survived to reach the quaternary facility.

6.2.2 Determine the relationship between transport methods to the hospital and outcome following severe TBI

The second research objective of this study was to determine the relationship between transport methods to IALCH and patient outcome following severe TBI. A statistically significant relationship exists between mortality and transport method to a level 1 facility ($p<0.001$). A large percentage of patients who did not survive admission at

IALCH were direct admissions suggesting improved patient outcome in patients who are stabilised at a base hospital prior to transportation to a level 1 facility. Direct admissions are associated with an increased mortality rate, with some patients having died within three days after arrival at IALCH. The results of this study also revealed a significant association between the method of transportation and length of stay ($p=0.004$). Patients admitted directly to IALCH had a statistically significant shorter length of stay compared to inter-hospital transfers.

6.2.3 Describe outcome predictors that predict mortality in severe traumatic brain injury

The final research objective is to describe outcome predictors that predict mortality in severe traumatic brain injury. Scoring systems such as NISS, RTS and GCS were included in this study. All scoring systems had good mortality prediction. However, this study revealed that NISS was the best predictor of mortality in all patients included in this study, regardless of their method of transportation. The most influential predictors of clinical outcome, such as demographics, GCS, hypotension, pupil response and CT scan findings, were extensively discussed in this study. The results of this study revealed that mostly young males between 21-35 years of age sustained severe traumatic brain injury; a large percentage of patients were not hypotensive on arrival at IALCH; however, 75% of patients who were hypotensive (SBP<90mmHg), did not survive suggesting a significant association between hypotension and mortality ($p=0.004$). Assessing pupil response was slightly challenging as a pupillary response was unable to be assessed in most patients due to uncontrollable factors such as peri-orbital oedema. More than half (52.5%) of patients who died presented with abnormal pupil response. An interesting finding in this study was that the association between hyperglycemia and mortality was borderline significant ($p=0.07$), which may be due to the small sample size.

6.3 Recommendations

The results of this study suggested that TBI remains a large burden of injury on the economy. Conducting further research regarding predictors of mortality in severe TBI in South Africa and the African continent is highly recommended as there is limited literature on this topic available within South Africa and the African continent. Another recommendation is to formulate a prediction-model that will predict patient outcome and mortality of severe traumatic brain injury. A prediction-model will assist healthcare providers in accurately predicting mortality in severe TBI. Ultimately, this will assist healthcare workers with decision-making in the pre-hospital environment with regard to triage in mass-casualty events, patient prognosis and transportation to a level 1 trauma facility.

6.4 Recommendation for future research

This research provides additional knowledge to the minimal literature available regarding severe TBI in the South African context. Future research could focus on exploring the morbidity of patients post-TBI, placing in perspective the cognitive burden of TBI on South Africans. Another opportunity for future research is to investigate the prevalence, outcome predictors and outcome analysis in paediatric patients. This research study revealed borderline significance between hyperglycemia and mortality, suggesting further research would be interesting with the need for larger numbers.

6.5 Limitations of the study

The first limitation of this study is that it did not investigate severe TBI in paediatrics (age<12 years). All patients above 12 years of age with a provisional diagnosis of ‘severe TBI’ were included in this study. In addition, the study included patients admitted into the only level 1 trauma facility in the province. Accordingly, the study findings may not be representative of outcome in other level 1 trauma facilities in South Africa. One of the objectives of this study were to describe patient longer-term outcome following severe TBI using the GOSE. The majority of patients were discharged from IALCH back to the base hospitals. The researcher was limited to only accessing records from IALCH and not from the surrounding base hospitals. It was, therefore, impractical to determine only patient outcome at hospital discharge since longer-term survival is unknown.

6.6 Conclusion

The burden of traumatic brain injury on quality of life in South Africa affects mostly young males, and there is no indication of this changing in the near future. Evidence emerged that severe TBI is predominantly caused by motor vehicle collisions. This study determined better patient outcome in patients transported to base hospitals, stabilised and later transferred to a level 1 trauma facility. As revealed by the study findings, the factors that best predict mortality include clinical predictors and scoring systems. In the pre-hospital environment, GCS is the most commonly utilised scoring system to predict mortality. A significant relationship exists between GCS 13-15 and decreased mortality, despite severe TBI on CT scan findings. NISS has proven to be the most reliable predictor of mortality in severe TBI. Clinical predictors, including hypotension, hyperglycemia and hypoxia, was included in this study. Hypotension demonstrated a significant association with mortality, despite the method of transportation to a level 1 facility.

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Annexure A: Letter of approval from IALCH trauma unit

HPCSA Accredited Trauma Training Unit of UKZN

health

Department:
Health
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Reference : DUT/Hardcastle/01-2020
Enquiries : Prof T C Hardcastle
30/01/2020

To Whom It May Concern:
DUT

Dear Sir / Madam

Re : Retrospective chart review study of Traumatic Brain Injury at IALCH: Blanca Hardcastle

This letter serves to confirm that the Trauma Registry at IALCH and the associated electronic medical records are pre-approved for retrospective chart review and prospective observational studies, including national and international collaborative and data-sharing studies, of routinely collected data by the Biomedical Research Ethics Committee of UKZN. As the Principal Investigator on that approval (BCA207-09) I confirm that I have permission to allow students access to the database for de-identified or anonymized studies. Ms Blanca Hardcastle will access this data under my supervision and as such permission to conduct the study is provided. No further gatekeeper permissions are required for this database.

Kind regards

Prof Timothy Craig Hardcastle
M.B., Ch.B.; M. Med. (Chir); PhD (UKZN); FCS (SA); Trauma Surgery (HPCSA)
Head of Clinical Dept: Trauma Surgery (Clinical Head: Trauma and Burns – KZN-DoH)
Director: IALCH Trauma Service
Director: Trauma Training Program – UKZN
Honorary Clinical Fellow: Department of Surgery, UKZN / Honorary Research Professor DUT

Annexure B: Letter of approval from University of Kwa-Zulu Natal Biomedical Research Ethics Committee

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05 March 2020

Dr Timothy Hardcastle
Trauma Unit, Private Bag X03
Mayville
4058

Dear Dr Hardcastle

PROTOCOL: Retrospective analysis of the Medicom and Trauma Unit databases at IALCH and PMB Trauma Units for the purposes of Audit and Review publications from the Unit.
REF: BCA207/09.

We wish to advise you that your letter received on 19 February 2020 submitting notification of the addition of co-investigator Dr S Sibuwa and Ms B Hardcastle to the above study has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee.

The committee will be advised of the above at its next meeting to be held on 14 April 2020.

Yours sincerely

Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

Annexure C: Data collection sheet template

		DEMOGRAPHICS						VITAL SIGNS (on admission)						PATIENT OUTCOME				
Case No:	Type of Transportation	Date of Admission	Age	Sex		GCS					PUPILS				GOSE			
					Eyes	Motor	Verbal	Saturation (%)	Pulse rate	BP	Left side	Right Side	HgT	Poor	Moderate	Good		

New Injury Severity Score	CT Scan Findings	Revised Trauma Score	Mechanism of injury	Injury Severity Score	Length of Stay		Complications			
						VAP	Re-operation	Aspiration	Rescan	Re-neuroprotect