# THE SPECTRUM AND CLINICAL OUTCOME OF CIVILIAN CEREBRAL GUNSHOT WOUNDS AT A MAJOR TRAUMA CENTRE IN SOUTH AFRICA


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**MBChB, ChM, MSc, PhD, MRCS(Ed)**


Submitted in fulfilment of the requirements for the degree of

**Doctor of Medicine (MD)**


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# Declaration: General

I, **Victor Kong**, declare that this research report is my own work. It is being submitted for the degree of **Doctor of Medicine** in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

The 27th day of October 2018

# Declaration: Plagiarism

I, **Victor Kong** (Student number: **2086207**) am a student registered for the degree of **Doctor of Medicine (MD)** in the academic year of **2018**.

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**Name of Student:** **Dr Victor Kong**

**Signature of Student:**

**Date**: 27/10/2018

**Name of Supervisor**: **Professor Damian Clarke**

**Signature of Supervisor:**

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# Declaration: Agreement by co-authors

By signing this declaration, the co-authors listed below agree to the use of the article(s) by the student as part of his/her Thesis/Dissertation/Research Report.

**<u>Article 1</u>:**

**<u>Kong VY</u>**, Odendaal JJ, Sartorius B, Clarke DL, Brysiewicz P, Jerome E, Bruce JL, Laing GL. Civilian cerebral gunshot wounds: a South African experience. *ANZ J Surg*. 2017: 87(3): 186-9. DOI: 10.1111/ans.13846.

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**<u>Article 2</u>:**

**<u>Kong VY</u>**, Clarke DL, Laing GL, Bruce JL, Brysiewicz P, Sartorius B, Odendaal JJ. Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality than in urban patients. *Eur J Trauma Emerg Surg*. 2017. DOI: 10.1007/s00068-017-0800.

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**Article 3**:

**Kong VY**, Oosthuizen GV, Sartorious B, Bruce JL, Laing GL, Weale R, Clarke DL. Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: The Pietermaritzburg experience. *Eur J Trauma Emerg Surg*. 2018;; 44(4):615-620. DOI: 10.1007/s00068-017-0835-1.

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**Article 4**:

**Kong VY**, Clarke DL, Oosthuizen GV, Esterhuizen T, Bruce JL, Laing GL, Odendaal JJ. Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: The Maritzburg Score. *Ann R Coll Surg Engl*. 2018; 100(2):97-100. DOI: 10.1308/rcsann.2017.0141.

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**Article 5**:

**Kong VY**, Weale R, Sartorius B, Oosthuizen GV, Bruce JL, Laing GL, Clarke DL. A raised serum lactate level is an independent predictor of in-hospital mortality in-patients with isolated cerebral gunshot wounds. *S Afr Med J*. 2018; 108(5):413-417. DOI: 10.7196/SAMJ.2018.v108i5.12837.

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**Article 6**:

**Kong VY**, Weale R, Sartorius B, Bruce JL, Laing GL, Clarke DL Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: a South African experience. *Emerg Med Australas*. 2018. DOI: 10.1111/1742-6723.12985.

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# Dedication

First and foremost, and above all, this dissertation is dedicated to the almighty God. Without his blessing of wisdom, knowledge, skills and perseverance, none of this would have been possible.

# Acknowledgement

I would like to express my greatest gratitude to my parents (CS Kong and KCL Kong), who have sacrificed much to allow me to pursue higher education and specialist surgical training. They have given much in their lives for me so I can have the opportunities they never had.

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# Abbreviations

| | |
|---|---|
| CHBAH | Chris Hani Baragwanath Academic Hospital |
| BREC | Biomedical Research Ethics Committee |
| CSI | Cervical Spine Injury |
| EMS | Emergency Medical Service |
| GCS | Glasgow Coma Scale |
| GSW | Gunshot wound |
| HVF | High-Velocity Firearm |
| KZN | KwaZulu-Natal |
| LVF | Low-Velocity Firearm |
| PMTS | Pietermaritzburg Metropolitan Trauma Service |
| RD | Rural District |
| TBI | Traumatic Brain Injury |
| UD | Urban District |

# Abstract

**Introduction**

Cerebral gunshot wounds (GSWs) are highly lethal injuries and are common in South Africa. Literature focusing on the injury spectrum and clinical outcome in the specific context of the developing world setting in South Africa is limited.

**Materials and Methods**

This Doctor of Medicine (MD) thesis is based on a series of retrospective studies undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. The regional trauma registry was used as the basis for the studies and was reviewed over a five-year period (January 2010 to December 2014). The thesis comprises six published papers in peer-reviewed journals which examine different aspects of cerebral GSWs within the South African context.

**Results**

A total of 102 patients were included in these studies in which 92% were male, with a mean age of 29 years. In *Chapter 1 (Article 1)*, we demonstrate that in our setting, cerebral GSWs occur primarily in young males who are predominantly victims of interpersonal violence involving low-velocity firearms, with self-harm and accidental injuries being uncommon. The overall mortality was high. *Chapter 2 (Article 2)* demonstrates that rural patients have disproportionally higher mortality compared with their urban counterparts, likely related to prolonged transfer time to definitive care. *Chapter 3 (Article 3)* demonstrates that for those patients who were transferred to our trauma centre, the Baragwanath mortality-prediction score accurately predicted non-survivors and was directly applicable to our patient cohort. *Chapter 4 (Article 4)* highlights that the Maritzburg score, based on the presence of visible brain matter and a GCS motor score < 5 on admission, allows simpler and more accurate identification of non-survivors. *Chapter 5 (Article 5)* demonstrates that a raised serum-lactate

level on presentation was closely correlated to adverse outcome and is an independent predictor of in-hospital mortality while *Chapter 6 (Article 6)* demonstrates that patients with isolated cerebral GSWs were highly unlikely to sustain concomitant cervical spine injury and therefore routine cervical spine immobilisation is unnecessary.

**Conclusions**

Cerebral GSWs are associated with high mortality, with rural patients having disproportionately higher mortality than their urban counterparts. Relevant prediction scores based on simple clinical parameters that are readily available in the resuscitation room, as well as a raised serum-lactate level are accurate in predicting non-survivors in our resource-constrained environment. Concomitant cervical spine injury in isolated cerebral GSW is extremely rare and routine cervical spine immobilisation is unnecessary. Efforts should therefore rather be directed at management strategies aiming to prevent secondary brain injury in order to optimise clinical outcome.

# Introduction

## Background

Globally, trauma remains the most common cause of mortality in people under 40 years of age and trauma victims often belong to the most economically active group in society [1, 2]. Worldwide, over 90% of trauma mortality occurs in developing countries [3]. Annually, over 1.4 million people worldwide die as a result of violent trauma [4]. While no country is completely immune from violence, South Africa has a notorious reputation for its high levels of violent crime [4,5]. South Africa is a developing country that has a unique history characterised by apartheid that created a society based on racial segregation, social injustice, inequalities and politically motivated violence [6]. Despite the establishment of democracy in 1994, South Africa continues to be plagued by an excessive burden of trauma, a large proportion of which is directly related to interpersonal violence [6-8]. The situation in South Africa was termed the 'malignant epidemic' by Muckart and this expression aptly describes the scale of the problem [7,8]. Annually, over 80,000 South Africans die as a result of trauma and over four million require hospital treatment following an injury [9]. Interpersonal violence is rife in almost every region of the country as a result of a complex web of socio-economic, political and historical factors [6]. Violent crime remains stubbornly high and homicide is now the commonest cause of death in young, adult males [2,10]. The homicide rate in South Africa is 37 per 100,000 of the population, which is 30 times higher than the United Kingdom and six times that of the United States [2,3]. Over 55 people are murdered in South Africa every day and these figures far exceed those for any other country which is not at war [2,5,11,12]. In a 2009 forensic study by the South African Medical Research Council (SAMRC), it was estimated that 98% of all firearm deaths were caused intentionally, and 88% of these were homicides [13,14].

In South Africa, there are approximately 4.5 million registered firearms documented to be in circulation [15]. However, it has been estimated that over 1 million firearms are held illegally

[15]. It has been suggested that theft and loss of firearms from both civilians and law enforcement agencies contributes to a significant proportion of the illegal firearms in circulation [16]. In 2006 alone, 3865 firearms were reported lost by the South African Police Service. Even though the common perception is that firearms are generally owned by South African law-enforcement agencies, there are, in fact, six times more firearms owned by civilians than by government agencies [16,17]. Efforts to curb firearm-related crime have been severely hampered by a lack of political will to enforce existing legislation [15]. Currently, South Africa continues to have one of the highest firearm-related mortality rates in the world [18,19]. Furthermore, the management of non-fatal firearm-related injuries is extremely costly and contributes a significant burden to the already overstretched healthcare system [19].

Cerebral gunshot wounds (GSWs) are a dramatic form of traumatic brain injury (TBI) which are commonly encountered in most major trauma centres across South Africa [20,21]. They are one of the most lethal forms of TBI and over 90% of victims will die before reaching hospital, and, of those who reach hospital alive, a further 50% will succumb in the resuscitation room [20,21,23-27]. Many survivors are disabled and require long-term rehabilitation which consumes significant resources [21,26]. Government rehabilitation facilities are inadequate and preclude many patients from receiving appropriate rehabilitation services [28]. In the United States (US), firearm-related violence has received increased scrutiny by the media and has dominated political debates in recent times [29,30]. This is in stark contrast to the situation in South Africa where it remains a largely neglected issue, and where public health policies usually prioritise infectious diseases such as HIV [31]. Cerebral GSWs attracted significant international media attention when US Congresswoman Gabrielle Gifford was shot in 2011 in Arizona [32]. Her remarkable recovery highlighted the need for evidence-based treatment algorithms for the management of these injuries [32]. Historically, the evidence for management of cerebral GSWs was largely based on the military experience from the Vietnam War [33]. However, the majority of cerebral GSWs encountered in the civilian population are of low-velocity type mechanisms and the associated pattern of injury differs from that in the military setting [24]. Furthermore, major improvements in pre-hospital and perioperative care, as well as technological advances in imaging and the development of trauma systems have resulted in vastly improved outcomes for trauma patients [34]. Most of the published literature on civilian cerebral GSW available to date is based on data from major US cities [22-25,27]. Given the differences in the healthcare systems between the US and South Africa and the resources available for trauma care, these findings may not always be applicable to our environment.

The excessive burden of trauma in South Africa has allowed many local surgeons to develop vast experience in many areas of trauma care [6]. Many of these surgeons, based in major academic trauma centres have made substantial contributions to the advancement of trauma care and are renowned internationally [6]. In general, the majority of TBI in South Africa are managed primarily by trauma surgeons with input from neurosurgeons in selected cases. This is a result of the shortage of neurosurgical services in South Africa [35-39]. Trauma surgeons in South Africa are general surgeons with subspecialist training and trauma surgery is currently a nationally recognised independent subspecialty [35,36]. These surgeons are based almost exclusively in the urban trauma centres and provide tertiary trauma services and support to rural hospitals within the catchment area [40]. However, a significant proportion of trauma patients reside in the rural areas and initial care is usually provided by the local district hospitals [40]. These are usually staffed by general practitioners and junior doctors with limited or no formal training in trauma care [41]. As with other traumatic injuries, cerebral GSW is a time-critical pathology that requires appropriate early management. The adequacy of this early management has a significant influence on the final clinical outcome for the patient. [42-44]. It is therefore important for frontline staff to be well versed on the initial management of these patients and to swiftly transfer them to definitive trauma care [42-45]. Paradoxically, despite the burden of firearm-related violence, very little is known regarding the current situation related to cerebral GSWs in South Africa

[20,46,47,48,49]. To date, there have only been two studies from South Africa which provide a description of the injury spectrum in adults and both were published over 10 years ago [20,46]. Both reports were from University of the Witwatersrand in Johannesburg [20,46]. The overall mortality rate reported by Stoffel, *et al.* at Chris Hani Baragwanath Academic Hospital (CHBAH), based on his series of 242 patients was 27%, while that from the study by Glapa, *et al.* from Milpark Hospital was 58% [20,46].

Given the significant burden of these injuries and the potential impact of initial management on the outcome for these patients, a thorough understanding of this injury in the South African context is important. Based on an understanding of the significant deficits in knowledge on this topic in both the national and international literature, this thesis aims to examine this injury in detail, with a specific focus on the initial resuscitation phase of patients with cerebral GSWs managed in an urban academic trauma centre in South Africa.

**Objectives**

The objectives of the research project on which the MD thesis is based are as follows:

1. To describe the spectrum and clinical outcome for patients who sustained cerebral GSWs in the civilian setting.

2. To describe the discrepancies in clinical outcomes between rural and urban patients who sustained cerebral GSWs.

3. To validate the Baragwanath mortality-prediction score for cerebral GSW in a similar patient population in KwaZulu-Natal.

4. To propose an alternative simplified mortality-prediction score based on clinical parameters for cerebral GSW that are immediately available in the resuscitation room.

5. To review the role of serum-lactate levels as a predictor of in-hospital mortality cerebral GSWs.

6. To review the role of cervical spine immobilisation with rigid collar in the initial management of patients with cerebral GSWs.

**Clinical Setting**

This was a series of retrospective reviews undertaken in the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. The regional trauma registry was reviewed for a five-year period, from January 2010 to December 2014. KwaZulu-Natal (KZN) is located on the east coast of South Africa, and has a population of over 11 million people [47]. It is the second-most populous province in South Africa and 50% of the population live in rural areas [47]. The PMTS provides definitive trauma care to the city of Pietermaritzburg, which is the capital of the province. The PMTS serves as the trauma referral centre for 19 rural hospitals within the western part of the province, and serves a total catchment population of over three million people. The catchment area is divided into two health districts: the urban district (UD), which includes the city of Pietermaritzburg and the surrounding suburban areas, and the rural district (RD), which includes all areas outside of the city's geographical boundaries. Approximately 4,000 trauma cases are admitted to the PMTS per annum, with over 50% having sustained penetrating trauma. This is a direct reflection of the high incidence of inter-personal violence and serious crime which is experienced throughout the province [48].

Ethics approval to maintain the trauma registry and to use data contained therein for these studies was provided by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (reference: BCA 221/13). This approval is renewed annually and is fully compliant with local Institutional review board (IRB) requirements. The primary researcher holds a current ICH Good Clinical Practice Certificate (06/03/2018): 003026708.

## Thesis Structure

This is an MD thesis by published work and comprises six chapters, each of which corresponds to a specific objective as outlined in the previous section. Each chapter contains the corresponding article which was published in peer-reviewed journals that are searchable on PubMed. This is followed by a final concluding chapter which provides a summary of the entire thesis.

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# Chapter 1

## Introduction

The first paper, titled ***'Civilian cerebral gunshot wounds: a South African experience'***, provides an overview of the spectrum and outcome of cerebral GSW as seen at our trauma centre in KZN. This sets the scene for the subsequent publications which interrogate other key aspects of cerebral GSWs in greater detail. This paper provides a contemporary overview and a comprehensive description of patient demographics, patterns of injury, and clinical status, and documents the clinical outcome of patients with cerebral GSWs managed in a major South African trauma centre.

## Key Findings

This study shows that the vast majority of those who sustained cerebral GSW are young, males. Interpersonal violence accounted for the majority of cases, with self-inflicted and accidental injury being uncommon. This differs from US studies in which many studies describe a relatively higher proportion of self-inflicted and accidental injury. It has also shown that even though cerebral GSWs are associated with significant mortality, those patients who survive to reach our trauma centre for definitive care generally do well and appear to have a reasonably good clinical outcome even in our resource-constrained environment.

## **Publication 1**

**Kong VY**, Odendaal JJ, Sartorius B, Clarke DL, Brysiewicz P, Jerome E, Bruce JL, Laing GL. Civilian cerebral gunshot wounds: a South African experience. *ANZ J Surg*. 2017: 87(3): 186-9. DOI: 10.1111/ans.13846.

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# Civilian cerebral gunshot wounds: a South African experience

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**Key words**
cerebral, civilian, gunshot wounds, mortality, outcome disparity.

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## Abstract

**Background:** Cerebral gunshot wounds represent one of the most lethal forms of traumatic brain injury, but there is a paucity of literature on the topic, especially from the developing world. We reviewed our experience and describe the spectrum and outcome of civilian cerebral gunshot wounds in a major metropolitan trauma centre in South Africa.
**Methods:** This was a retrospective study of all patients with isolated cerebral gunshot wounds managed by the Pietermaritzburg Metropolitan Trauma Service over a 5-year period from 2010 to 2014.
**Results:** One hundred and two patients were included, 92% (94/102) were male and the mean age was 29 years. Fifty-four per cent (55/102) of all patients were from urban areas. The mean time from injury to arrival was 6 h (standard deviation: 5) for urban patients and 15 h (standard deviation: 5.2) for rural patients ($P < 0.001$). Ninety-four per cent (94/102) of all injuries were related to interpersonal violence and involved low velocity firearms. Twenty per cent of all patients (20/102) had a Glasgow Coma Scale 3–8, 20% (20/102) 9–12 and 61% (61/102) 12–15. All 102 patients underwent computed tomography scans. Thirty per cent (31/102) required neurosurgical interventions. The overall mortality rate was 22% (22/102). There was a significant difference in mortality between urban and rural patients (9% versus 36%, $P < 0.001$).
**Conclusions:** Cerebral gunshot wounds are associated with significant mortality and protracted delay to definitive care is common in our setting. Those who survive the delayed transfer to definitive care generally do well and have reasonably good clinical outcomes.

## Introduction

Cerebral gunshot wounds (GSWs) represent one of the most lethal forms of traumatic brain injury (TBI).[1–6] Over 90% of victims die before reaching hospital, and a further 50% die in the resuscitation room.[5,6] Civilian cerebral GSWs are relatively uncommon outside South Africa[1] and United States.[7] It is evident from the literature that the mechanism of injury ranges from interpersonal violence to self-harm and that the spectrum of injury, management and outcome vary considerably according to geographical location.[8,9] There is currently a paucity of literature describing the situation in South Africa, a developing country with a heavy burden of trauma, where firearm-related injury has reached an epidemic proportion.[10] The objective of this study was to describe the spectrum and outcome of cerebral GSWs managed by a major metropolitan trauma centre in South Africa.

## Methods

### Clinical setting

This was a retrospective study undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Our electronic regional trauma registry was reviewed over a 5-year period from January 2010 to December 2014. Ethics approval for this study and for maintenance of the registry was formally endorsed by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (reference: BE 207/09). The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of KwaZulu-Natal (KZN) province. It also serves as the major trauma referral centre for 19 other rural hospitals within the province, with a total catchment population of over 3 million. The catchment area is divided into two distinct health districts. The urban district (UD) includes the city of Pietermaritzburg and the surrounding suburban areas. The rural district (RD) includes all areas outside the UD geographical boundaries, with local rural hospitals providing basic, non-specialist healthcare. Urban patients are transported by the Emergency Medical Service (EMS) ambulance directly to our trauma centre, while rural patients are transported to the nearest healthcare facilities within the catchment area and subsequently referred to our trauma centre. Approximately 3000 trauma cases are admitted to the PMTS per annum, with over 40% penetrating trauma. This is a direct reflection of the high incidence of firearm-related interpersonal violence and criminal activities experienced throughout the entire province.

### Prehospital Emergency Medical Service (EMS)

South Africa is unique in that it operates a 'two-tier' prehospital EMS system, one for the public and the other for the private sector.[11] The levels of training and experience of EMS personnel are extremely heterogeneous within the public sector. All of our patients in this study were transported by the EMS road ambulances that belonged to the public sector. Literature from South Africa on the level of care in the prehospital phase is limited. Due to the haphazard nature of this relatively immature system, delay in evacuation and transportation is common. At present, the general approach in the prehospital phase is 'scoop and run'. This minimalist approach stems from the philosophy of selective conservatism that has underpinned trauma care in South Africa for decades, primarily out of necessity due to resource constraints. Victims are immediately evacuated to the nearest healthcare facilities with minimal interventions on scene. There is also a chronic shortage of EMS ambulances throughout the province.

### The study

The initial management of all patients with cerebral GSWs closely follows the Advanced Trauma Life Support (ATLS) principles. All patients who sustained a single, isolated cerebral GSW were included in the study. Those with concurrent GSWs to other body regions were excluded. Those patients who were dead in transit or dead on arrival were taken directly to the mortuary and were not considered further. Basic demographic data were reviewed. Where available, specific information was sought regarding the geographical locations of the incident within the catchment area, as well as the documented approximate time of injury (if known). Further data review included the mode of injury (assault, suicide or accident), types of firearms, vital signs (physiological parameters on arrival), physical examination findings, Glasgow Coma Scale (GCS) and the final clinical outcome. The conventional classification of injury severity based on GCS was used to group all patients into three categories: mild (13–15), moderate (9–12) and severe (3–8).

### Statistical analysis

Data were processed and analysed using Stata 13.0 (StataCorp LP, College Station, TX, USA). Continuous variables were summarized using mean and standard deviation (SD). If there was evidence of skewing/asymmetry for a continuous variable then the median and interquartile range were presented instead. Differences in means of continuous variables such as age by urban/rural setting were assessed using the Student's *t*-test. Association between categorical variables and urban/rural setting were assessed using the Pearson chi-squared ($\chi^2$) test or Fisher's exact if expected cell count with fewer than observations. The significance cut-off used was 5%.

## Results

### Demographics

During the 5-year study period, a total of 102 patients with isolated cerebral GSWs were included. Ninety-two per cent (94/102) were male and the mean age was 29 years (SD: 8 years). Fifty-four per cent (55/102) of all patients were from the UD who were transported directly to our trauma centre. The remaining 46% (47/102) from the RD had initially been transported to their respective rural hospitals and subsequently transported to our trauma centre. The time of injury was available in 60% (61/102) of patients. The mean time from injury to arrival for all patients was 11 h (SD: 7). The mean time from injury to arrival was 6 h (SD: 5) for patients from UD and 15 h (SD: 5.2) for patients from RD ($P < 0.001$).

### Pattern of injury

Ninety-four per cent (94/102) of injuries were related to interpersonal violence (assaults). The remaining 6% (6/102) were attempted suicides, all of whom were male. Ninety-eight per cent (100/102) involved the use of low velocity firearms, and the remaining 2% (2/102) were high velocity firearms.

### Clinical status

The mean (SD) values of physiological parameters on arrival were as follows: heart rate: 85/min (24), systolic blood pressure: 124 mmHg (22), temperature: 36°C (1). The mean (SD) GCS on arrival was 12 (5). Twenty per cent (20/102) had a GCS 3–8, 20% (20/102) 9–12 and 61% (61/102) 13–15. Thirty per cent (31/102) of all patients had visible brain matter oozing from the wound. All 102 patients underwent computed tomography (CT) scans. Findings (in order of decreasing frequency) were as follows: haemorrhagic contusion (92), cerebral oedema (80), intracerebral haemorrhage (71), subarachnoid haemorrhage (48), intraventricular haemorrhage (35), subdural haematoma (4), epidural haematoma (3). Twenty-two had a retained bullet *in situ*.

Thirty percent (31/102) required neurosurgical interventions. Twenty-eight (90%) of these 31 patients underwent debridement and/or elevation of depressed skull fracture and three required formal craniotomy for haematoma evacuation. The remaining 71 patients who were managed non-operatively received general neurosupportive care.

### Clinical outcome

Of the 102 patients, 22% (22/102) died during the admission. The remaining 80 patients (78%) survived to discharge to rehabilitation. The mean (SD) GCS on discharge of all 80 survivors was 14 (2). Seventy per cent had a GCS 13–15, and the

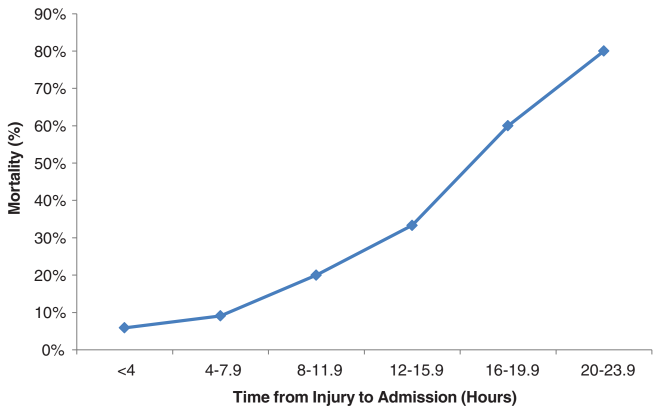


**Fig. 1.** Mortality in relation to time from injury to admission for all 61 patients.

remaining 30% had GCS 9–12. Of the 61 patients with documented time of injury, 16 died. Figure 1 shows the mortality trend in relation to time from injury to arrival for all 61 patients with known time of injury.

## Rural versus urban patients

Direct comparison was made between all rural and urban patients in terms of demographics, patterns of injury, clinical status and outcome. This was summarized in Table 1. There was a significant difference in mortality between urban and rural patients (9% versus 36%, $P < 0.001$).

# Discussion

Cerebral GSWs are generally uncommon outside the military setting.[1] Historically, the management of civilian cerebral GSWs was based on the collective experience from the Vietnam War and most literature documenting the contemporary experience in the civilian populations is primarily from the United States.[1–6] Our current study in South Africa described a population of young males that were predominantly victims of interpersonal violence involving low velocity firearms, with self-harm being uncommon in our setting. Most importantly however, our results suggested that the majority of patients experienced a protracted time (mean of 11 h) from injury to definitive care, with mortality increasing exponentially with time delay. There was a disproportionately higher mortality rate among rural patients.

Rapid evacuation of trauma victims to specialist trauma centre for definitive management has long been recognized as critical to outcome.[12] Furthermore, the literature has consistently shown that rural trauma patients have a higher mortality than their urban counterparts.[13] The differences in quality of prehospital care, delay in transport and prolonged discovery time have been suggested as possible contributing factors.[14] With continued improvement in highly sophisticated and organized trauma systems throughout the developed world, coupled with availability of advanced imaging and improved neurosurgical techniques, the outcome of survivors has much improved over the past decade.[8] This is typified by the recent example of US congresswoman Gabrielle Giffords.[8]

This is in stark contrast to the situation in South Africa, where the resources allocated to manage the huge burden of trauma is perennially insufficient. Outside the few major metropolitan trauma centres, almost all rural hospitals are often understaffed and ill equipped for managing trauma, necessitating transfer to the

**Table 1** Comparison between rural and urban patients

| | Rural ($n$ = 47) | % | Urban ($n$ = 55) | % | $P$-value |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Mean age (years) (SD) | 30 (10) | | 29 (6) | | 0.467 |
| Male | 42 | 89 | 52 | 95 | 0.465 |
| Female | 5 | 11 | 3 | 5 | |
| Weapons | | | | | |
| Low velocity | 46 | 98 | 54 | 98 | 1 |
| High velocity | 1 | 2 | 1 | 2 | |
| Injury | | | | | |
| Assaults | 42 | 89 | 54 | 98 | 0.092 |
| Suicide | 5 | 11 | 1 | 2 | |
| Mean (SD) time from injury (h) | 15 (5) | | 6 (5) | | <0.001* |
| Admission clinical status | | | | | |
| Median heart rate (per min) (IQR) | 81 (60–102) | | 82 (71–100) | | 0.314 |
| Median systolic blood pressure (mmHg) (IQR) | 125 (113–145) | | 121 (104–130) | | 0.017* |
| Mean temperature (°C) (SD) | 36 (1) | | 36 (1) | | 0.249 |
| Median admission GCS (IQR) | 14 (4–15) | | 15 (12–15) | | 0.022* |
| GCS < 8 | 13 | 28 | 7 | 13 | 0.058 |
| GCS ≥ 8 | 34 | 72 | 48 | 87 | |
| Visible brain matter | 21 | 45 | 10 | 18 | 0.004* |
| Clinical progress | | | | | |
| Neurosurgical interventions | 14 | 30 | 17 | 31 | 0.902 |
| Intensive care admission | 3 | 6 | 4 | 7 | 0.859 |
| Clinical outcome | | | | | |
| Mortality | 17 | 36 | 5 | 9 | 0.001* |
| Median length of stay (days) (IQR) | 5 (2–9) | | 5 (3–7) | | 0.917 |
| Mean discharge GCS (SD) | 14 (2) | | 14 (2) | | 0.698 |

*$P$ < 0.05. GCS, Glasgow Coma Scale; IQR, interquartile range; SD, standard deviation.

metropolis. The problem of resource constraints is particularly apparent in the overburdened and inefficient prehospital EMS network, which often results in prolonged delay in trauma patients reaching definitive care. South Africa is unique in that the prehospital EMS operates a two-tier system (one public and one private).[11] The organization is somewhat haphazard compared with most of the developed world and the level of experience in EMS personnel within the public sector is extremely heterogenous.

Patient outcome specifically pertaining to cerebral GSWs and the relationship with transport time has never been reported in literature in the developing world. The only two studies to date were by Stoffel *et al.* from Baragwanath Hospital[1] (public institution), and Glapa *et al.*[15] from Milpark Hospital (private institution), both in Johannesburg. Stoffel *et al.* reported an overall mortality of 27%,[1] while mortality from the study by Glapa *et al.* was 58%.[15] There were no available data on prehospital transport time to definitive care or the demographics of their patients. The mortality rate from the private institution was double that reported from the public institution.[1,15] This is most likely related to the difference between the two prehospital EMS systems. With the modern and efficient EMS available in the private sector (comparable to the developed world), patients with severe injuries are more likely to survive to reach hospital and undergo definitive management, despite the devastating nature of their injury.

Most contemporary literature from the developed world places heavy emphasis on predictors of mortality[16–18] in order to aid identification of potentially salvageable patients. Numerous prognostic indicators have been proposed, including both clinical and radiological features. At present, there is no specific classification system based on CT findings alone in the setting of cerebral GSWs. Cerebral GSWs are undoubtedly associated with significant mortality, and over 90% of victims die before reaching the hospital.[1,5,6] Of those who survive to hospital, significant proportions die in the trauma resuscitation room.[5,6] However, mortality rates reported in the literature vary considerably and range from 30 to 80%.[1–6] Our study showed a mortality of 22%, which is similar to that reported by Stoffel *et al.* It is likely that the vast majority of our patients were ‘selected out’ due to protracted prehospital delay and did not survive long enough to reach our trauma centre. Due to current legislation, data from the forensic department on those patients who expired during transit were difficult to obtain and therefore not included in this study. However, those who survived to reach definite care in our setting were most likely to have sustained injuries that were compatible with survival.

Despite the generally perceived negative outlook of patients with cerebral GSWs, approximately 70% of our survivors had a GCS between 12 and 15 on discharge. Although our study was limited by the lack of long-term neurological outcome data and functional status of survivors, patients who survived delay to definite care even in our severely resource constrained environment appeared to have reasonably good clinical outcome. In our opinion, these patients should not be denied treatment based solely on certain clinical or radiological features. Management must be individualized in order to optimize the outcome for these patients. Further study is required to explore the potential multitudes of reasons for delayed presentation within the trauma system in order to improve patient outcomes in our setting.

## Conclusions

Cerebral GSWs are associated with significant mortality. Delay to definitive care is common in our setting, with rural patients having disproportionately higher mortality. Those who survive delay to definitive care generally do well and appear to have reasonably good clinical outcome.

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# Chapter 2

## Introduction

The second paper, titled ***'Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality than in urban patients'***, examines the issue of how access to care may impact on clinical outcome by comparing urban patients who sustain a cerebral GSW with their rural counterparts in KZN. Rural trauma patients are known to be compromised in comparison to their urban counterparts by their remoteness from major trauma centres and their relative inability to access appropriate healthcare resources. This may well translate into worse outcomes for equivalent injuries. The challenge for the trauma system in a province such as KZN is to overcome the limitations imposed by distance and to deliver consistent, high-quality trauma care over a large geographical area. This paper highlights and attempts to quantify the impact of this so-called 'tyranny of distance' on the clinical outcomes of a specific injury and further explore possible options in attempting to ameliorate these obstacles.

## Key Findings

Rural patients with cerebral GSWs have a significantly longer transfer time, lower GCS on arrival and higher mortality than their urban counterparts. As the current trauma system dictates that victims are transported initially to the nearest rural district hospital regardless of the institution's capability, and subsequently transferred to our trauma centre, significant delay is likely to be a major contributor to the higher mortality. Major shortages of appropriately trained prehospital paramedics and the haphazard organisation of the prehospital emergency medical service (EMS) are likely to be contributory to further delays in transfer of rural patients. Investment in the reorganisation of the current trauma system and expansion in prehospital EMS are likely to be important interventions in improving outcome in these patients.

**Publication 2**

**Kong VY**, Clarke DL, Laing GL, Bruce JL, Brysiewicz P, Sartorius B, Odendaal JJ. Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality than in urban patients. *Eur J Trauma Emerg Surg*. 2017.. DOI: 10.1007/s00068-017-0800.

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ORIGINAL ARTICLE

# Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality rates than in urban patients

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**Abstract**

*Introduction* This study focuses on a specific and often dramatic injury, namely gunshot wounds (GSW) of the head in order to determine whether there is a discrepancy in outcome between patients who sustain their injury in a rural setting and those who sustain it in an urban setting.

*Materials and methods* This study involves a retrospective review of our prospectively maintained regional electronic trauma registry. All patients who sustained a cerebral GSW from January 2010 to December 2014 were reviewed.

*Results* During the 5-year study period, a total of 102 patients sustained an isolated cerebral GSW. Ninety-two per cent (94/102) were male and the mean age was 29 years. Ninety-four per cent (94/102) of injuries were related to interpersonal violence. Of the 102 patients in the study, 54% (55/102) were urban and were transported directly to our trauma centre. The remaining 46% (47/102) were rural and were transported to a rural district hospital prior to being referred to our trauma centre. The time of injury was available in 60% (61/102) of patients. The mean time from injury to arrival for all patients was 11 h (SD 7). The mean time from injury to arrival was significantly shorter for urban versus rural, 6 h (SD 5) and 15 h (SD 5), respectively ($p < 0.001$). The median admission GCS score was significantly lower in rural compared to urban patients ($p = 0.022$). The need for neurosurgery, need for ICU admission or length of hospital stay was not significantly different between rural and urban patients. Rural patients have a fourfold higher mortality compared with urban patients (36 vs 9%, $p = 0.001$). Amongst survivors, there was no significant difference in median length of hospital stay or mean discharge GCS.

*Conclusions* Cerebral GSWs are highly lethal injuries associated with significant mortality. Rural patients have a significantly longer transfer time, lower GCS on arrival and higher mortality than urban patients. Efforts should be directed at improving the pre-hospital EMS system in order to reduce delay to definitive care so that patient outcome can be optimised.

**Keywords** Cerebral gunshot wound · Gunshot wound of the head · Rural · Urban

## Introduction

According to the Lancet commission on global surgery, surgical conditions account for approximately 30% of the global burden of disease, yet it is estimated that two-thirds of the world's population cannot access safe surgery and anaesthesia. This translates into significant preventable morbidity and mortality [1]. Globally, it has long been recognised that within countries, there are major discrepancies in access to healthcare, and urban centres tend to be better served than more rural [2–5] centres. This is especially the case in South Africa, which is classified as a low middle-income country (LMIC). The literature has also consistently shown that globally, rural trauma patients have higher mortality and worse outcome than their urban counterparts.

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Several reasons for this discrepancy have been postulated, but the literature on rural trauma outcomes in the South African context is limited. Since the advent of democracy in South Africa, substantial efforts have been made to address the deficits in rural healthcare, but much of this has been directed towards maternal health, child health and infectious diseases. Trauma is a surgical disease and has nevertheless remained a neglected epidemic [5–8]. As the AIDS pandemic is brought under control, it is expected that the burden of disease due to trauma and other surgical conditions will increasingly be recognised as a major problem. However, the capacity to deliver surgical care in rural areas in South Africa appears to have deteriorated and the burden of trauma in rural areas, their relationship between outcomes and the geographical location remains unclear. An evidence-based platform to motivate for increased attention to developing and enhancing surgical capacity in rural South Africa is thus a current priority. This study focuses on a specific and very dramatic injury, namely gunshot wounds (GSW) of the head. A cerebral GSW is a highly time-dependent injury and long delays to appropriate care exacerbate secondary brain injury [9–11]. This study was designed to examine whether any discrepancies exist in the outcomes for this injury based on whether the patient sustained the injury in a rural or an urban setting.

## Materials and methods

### Clinical setting

This study was a retrospective review of a prospectively maintained regional electronic database. It was undertaken in the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Our electronic regional trauma registry was reviewed for the 5-year period from January 2010 to December 2014. Ethics approval to maintain this database has been granted by the Biomedical Research Ethics Committee (BREC) of the University of Kwa-Zulu Natal (BE221/13 and BE 207/09). KwaZulu-Natal is located on the east coast of the country and has a population of over 11 million. Fifty per cent of the population live in the rural areas. The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of Kwa-Zulu Natal (KZN) province. It is one of the largest trauma centres in the province and also serves as the referral centre for 19 rural hospitals within the province, with a total catchment population of over three million. The catchment area is divided into two distinct health districts. The urban district (UD) includes the city of Pietermaritzburg and the surrounding suburban areas. The rural district (RD) includes all areas outside the geographical boundaries of the city of Pietermaritzburg. In the RD, district hospitals provide basic, non-specialist healthcare. Urban patients are transported by ambulance directly to our trauma centre, while rural patients are transported to the nearest healthcare facilities within the catchment area and subsequently referred to our trauma centre. There is a chronic shortage of ambulances within the province, and delays in evacuation of victim and transportation are common [10]. Approximately 3000 trauma cases are admitted to the PMTS per annum, with over 50% being due to penetrating trauma. This is a direct reflection of the high incidence of interpersonal violence and criminal activities through the entire province.

### Prehospital emergency medical service (EMS)

South Africa operates a ‘two-tier’ pre-hospital EMS system, consisting of a public sector service and a private service [8]. All the patients in this study were transported by the public sector EMS. The available literature on the pre-hospital burden of trauma in KZN suggests that the system is overwhelmed and has inadequate command and control systems. In addition, the level of training and experience of the public service EMS personnel is extremely heterogeneous. All this translates into delays in both evacuation and transportation of rural trauma patients. Once a patient has been retrieved he is usually evacuated to the nearest healthcare facility. This may not be the most appropriate facility and attempts to develop a more robust trauma system are ongoing [8].

### The study

All patients who sustained a single, isolated cerebral GSW were included in this study. Those with concurrent GSWs to other body regions were excluded. Basic demographic data were reviewed. Specific information was sought regarding the geographical locations of the incident within the catchment area, as well as the time of injury, and the ambulance transport time from location of incident to our trauma centre. Patients who sustained the injury within the UD were classified as ‘urban’, while those with injuries within the RD were classified as ‘rural’ patients. Further data review included the mode of injury namely assault, suicide or accident, the types of firearm, vital signs on arrival, physical examination findings, Glasgow Coma Scale (GCS) and the final clinical outcome. The conventional classification of injury severity based on GCS was used to group all patients into three categories: mild [13–15], moderate [9–12] and severe [3–8].

### Statistical analysis

Data were processed and analysed using Stata 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Continuous variables were summarised using mean and standard deviation (SD). If evidence of skewing/asymmetry was found then median and interquartile range (IQR) presented instead. Differences in means of continuous variables such as age by urban/rural setting were assessed using the student's *t* test. Association between categorical variables and urban/rural setting was assessed using the Pearson Chi squared ($\chi^2$) test or Fishers exact if expected cell count with fewer than observations. Significance cut-off used was 5%.

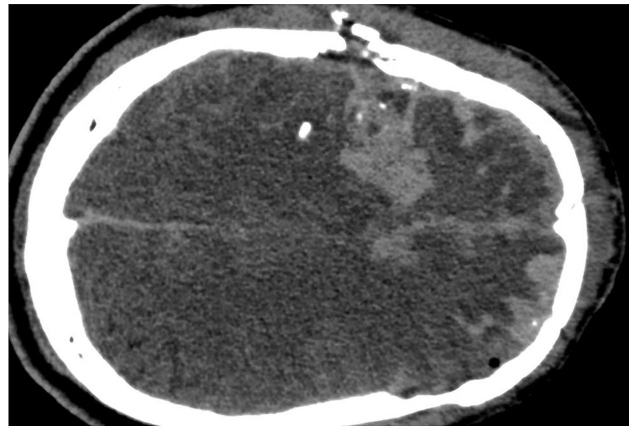

**Fig. 2** Axial CT image of left temporo-parietal GSW

## Results

### Description of cohort

During the 5-year study period, a total of 102 patients sustained an isolated cerebral GSW. Ninety-two per cent (94/102) were males and the mean age was 29 years. Ninety-four per cent (94/102) of injuries were related to interpersonal violence (assaults). The remaining 6% (6/102) were attempted suicides, all of whom were males. Ninety-eight per cent (100/102) involved the use of low-velocity firearms (LVF), and the remaining 2% (2/102) were high-velocity firearms (HVF). Figures 1, 2 and 3 show typical CT scans of patients with a cerebral GSW.

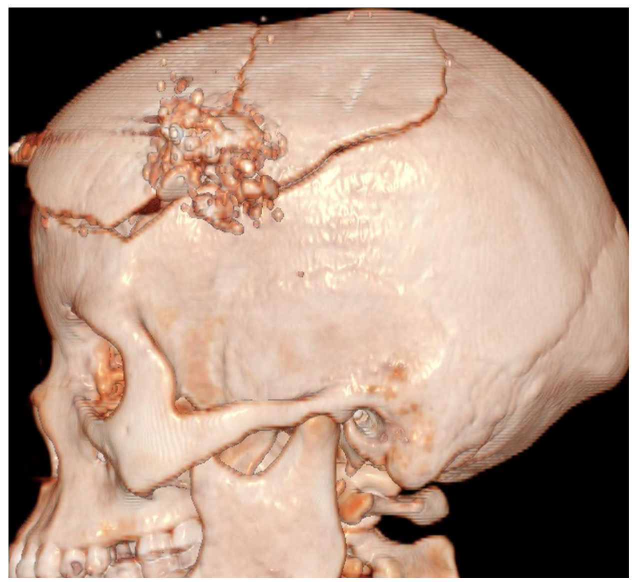

**Fig. 3** 3D reconstruction of left fronto-temporal GSW

### Rural vs urban patients: demographics

Of the 102 patients in the study, 54% (55/102) were from the UD and were transported directly to our trauma centre. The remaining 46% (47/102) were from the RD and had initially been transported to a rural district hospital prior to being referred to our trauma centre. The time of injury was available in 60% (61/102) of patients. The mean time from injury to arrival for all patients was 11 h (SD 7). The mean time from injury to arrival was significantly shorter for UD versus RD, 6 h (SD 5) and 15 h (SD 5), respectively ($p < 0.001$). Table 1 summarises the demographics, weapons, injury pattern and the time to definitive care.

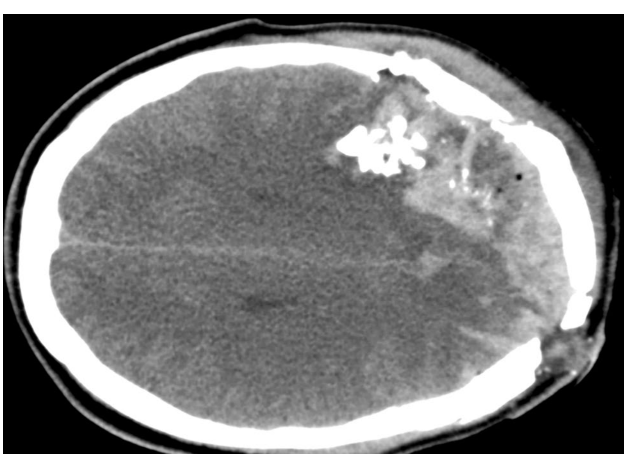

**Fig. 1** Axial CT image of trans-frontal GSW

### Rural vs urban patients: clinical status and progress

Table 2 summarises the comparison between rural and urban patients in terms of admission clinical status and clinical progress. The median admission GCS score

**Table 1** Comparison of demographics, weapons, injury pattern and the time to definitive care between rural and urban patients with cerebral GSWs

| | Rural ($N = 47$) | % | Urban ($N = 55$) | % | $p$ value |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Mean (SD), age (years) | 30 (10) | | 29 (6) | | 0.467 |
| Male | 42 | 89 | 52 | 95 | 0.465 |
| Female | 5 | 11 | 3 | 5 | |
| Weapons | | | | | |
| Low velocity | 46 | 98 | 54 | 98 | 1.000 |
| High velocity | 1 | 2 | 1 | 2 | |
| Injury | | | | | |
| Assaults | 42 | 89 | 54 | 98 | 0.092 |
| Suicide | 5 | 11 | 1 | 2 | |
| Mean (SD) time from injury (h) | 15 (5) | | 6 (5) | | <0.001 |

**Table 2** Comparison of admission clinical status and clinical progress between rural and urban patients

| | Rural ($N = 47$) | % | Urban ($N = 55$) | % | $p$ value |
|---|---|---|---|---|---|
| Admission clinical status | | | | | |
| Median (IQR), heart rate (per min) | 81 (60–102) | | 82 (71–100) | | 0.314 |
| Median (IQR), systolic BP (mmHg) | 125 (113–145) | | 121 (104–130) | | 0.017 |
| Mean (SD), temperature °C | 36 (1) | | 36 (1) | | 0.249 |
| Median (IQR), admission GCS | 14 (4–15) | | 15 (12–15) | | 0.022 |
| GCS <8 | 13 | 28 | 7 | 13 | 0.058 |
| GCS ≥8 | 34 | 72 | 48 | 87 | |
| Visible brain matter | 21 | 45 | 10 | 18 | 0.004 |
| Clinical progress | | | | | |
| Neurosurgical procedure | 14 | 30 | 17 | 31 | 0.902 |
| Median length of stay (in days) | 5 (2–8) | | 5 (2–6) | | 0.300 |
| ICU | 3 | 6 | 4 | 7 | 0.859 |

**Table 3** Comparison of overall in-hospital mortality between rural and urban patients

| | Rural ($N = 47$) | % | Urban ($N = 55$) | % | $p$ value |
|---|---|---|---|---|---|
| Clinical outcome | | | | | |
| Non survivors | 17 | 36 | 5 | 9 | 0.001 |
| Survivors | 30 | 64 | 50 | 91 | |
| Median (IQR), length of stay (days) | 5 (2–9) | | 5 (3–7) | | 0.917 |
| Mean (SD), discharge GCS | 14 (2) | | 14 (2) | | 0.698 |

was significantly lower in the rural patients compared to urban patients ($p = 0.022$). The need for neurosurgical procedure, ICU admission or length of hospital stay was not significantly different between rural and urban patients.

### Rural vs urban patients: clinical outcome

Table 3 summarises the difference in outcome between rural and urban patients. Rural patients have a fourfold higher mortality compared with urban patients (36 vs 9%, $p = 0.001$). Amongst survivors, there was no significant difference in median length of hospital stay or mean discharge GCS. The deaths are summarised in Table 4.

## Discussion

A cerebral GSW is one of the most lethal forms of traumatic brain injury [9–16]. In the civilian setting, it typically affects the young and economically active part of the population and is associated with significant morbidity and mortality [9, 10]. Over 90% of victims will die prior to reaching hospital, and a further 50% die in the resuscitation room [9, 10]. Numerous clinical factors may influence the outcome of these injuries. These include the cause of injury (suicide, assault or accident), the type of weapon, the path of the bullet and admission GCS. Our data suggest that the injury pattern is similar in the urban and rural patients. The weapons used were

**Table 4** Comparison of deaths between rural and urban patients

| Characteristics | Rural ($N = 17$) | % | Urban ($N = 5$) | % | $p$ value |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Mean age (years) | 29 | | 31 | | 0.467 |
| Male | 17 | 100 | 5 | 100 | 0.465 |
| Female | 0 | 0 | 0 | 0 | |
| Cause of death | | | | | |
| Structural brain injury | 3 | 18 | 0 | 0 | 0.558 |
| Nosocomial pneumonia | 10 | 59 | 4 | 80 | 0.386 |
| Other nosocomial sepsis | 1 | 6 | 0 | 0 | 0.468 |
| Unknown | 3 | 18 | 0 | 0 | 0.558 |
| Time to death | | | | | |
| <1 week | 10 | 59 | 1 | 20 | 0.126 |
| >1 week | 7 | 41 | 4 | 80 | |

overwhelmingly low-velocity hand-guns in both groups. This implies that we have identified a group of demographically similar patients with similar injuries, yet with a discrepant outcome. This strongly suggests that the reason for the discrepancy in outcome is related to an extraneous factor and our data suggest that this factor is rural origin as opposed to urban origin of the patient. The prolonged retrieval time and delays to definitive care associated with rural trauma almost certainly account for this discrepancy in outcomes. The rapid evacuation and transfer of these patients to a specialist trauma centre capable of definitive care is essential if one wishes to achieve an optimal outcome [3–5]. In countries with mature trauma systems where patients receive timely and appropriate treatment, reasonably good clinical outcomes can be expected. This is typified by the relatively good outcome achieved in the case of US congresswoman Gabrielle Giffords who survived an assassination attempt thanks to a mature and efficient trauma system [11].

Trauma in South Africa has been described as the malignant epidemic. Despite the advent of democracy the levels of trauma in the country have remained stubbornly high. Of major concern is that a great deal of this trauma is interpersonal [9–16]. In addition, interpersonal violence as a mechanism of trauma in South Africa is not restricted to urban conurbations but is also common in rural areas, as is shown in this audit. In other countries interpersonal violence is very much a feature of urban areas rather than rural ones [3–5].

Although we have shown that suicide attempts were more common in the rural population, the pattern of injury is largely similar to the urban population, with low-velocity firearms being the most common weapon used. A cerebral GSW is a highly time-dependent injury. Delays in appropriate treatment exacerbate secondary brain injury. Prolonged extraction and transfer times will translate into worse outcomes. The international literature has consistently shown that injuries sustained in rural areas are associated with higher mortality and worse outcome rates than the equivalent injury sustained in an urban setting [3–5]. Esposito et al. from Washington demonstrated that the crude mortality rate for trauma patients in rural settings was three times that of patients from urban areas [2]. Similarly Gomez et al. from Ontario showed that there was a threefold increase in mortality among patients injured in regions with limited access to specialised trauma care. There are many potential explanations for these observed discrepancies, which include differences in the quality of pre-hospital care, delays in transport and prolonged extraction times [4].

KwaZulu-Natal is the largest and most populous province of South Africa and has a population of over 11 million people of whom half reside in rural areas [7, 8]. Although a pre-hospital emergency medical service (EMS) exists, it less well organised than comparable services in high-income countries (HIC) and it is relatively under resourced [7, 8]. Our data have shown that the mean transport time for rural patients were significantly longer than their urban counter part. Moreover, rural patients tend to have a lower GCS on arrival. This is most likely related to prolonged extraction and transfer times, which exacerbate secondary brain injury due to hypoxia, hypotension and hypoglycaemia.

Rural patients have a fourfold increase in mortality compared with their urban counterparts. There were two main causes of death in this study. Early deaths (within 1 week) are likely to reflect the severity of the underlying brain injury whilst late deaths (beyond 1 week) are usually reflective of death due to nosocomial sepsis. This is especially relevant in our developing world setting where resources for specialised rehabilitation facilities are lacking. Furthermore, although not statistically significant, early deaths appeared to be more common in rural patients.

While cynics may argue that the 'devil of distance' is difficult to overcome, investing in the reorganisation of the EMS to improve rural extraction and retrieval times has been shown to improve outcome in rural trauma patients [13]. Literature from HIC also shows that the implementation of a rural trauma network results in improved outcomes for rural patients [14, 15]. While the reasons behind the higher mortality rate for rural trauma patients are certainly multifactorial, efforts should be directed towards improving the EMS. This will hopefully ensure more rapid transfer of rural trauma patients to a centre capable of delivering appropriate care and improve patient outcomes.

## Conclusions

Cerebral GSWs are highly lethal injuries associated with significant mortality. Rural patients have a significantly longer transfer time, lower GCS on arrival and higher mortality. Efforts should be directed at improving the pre hospital EMS system in order to reduce delay to definitive care so that patient outcome can be optimised.

#### Compliance with ethical standards

**Conflict of interest** We received no funding for this research and have no conflicts of interest to declare.

**Ethical approval** We have the necessary ethical approval for this study from the Biomedical Research Committee (BREC) of the University of KwaZulu-Natal (BCA221/13). We have ethics approval to keep and use this database (BE 207/09, 221/13).

**Author contributions** VYK: analysis and drafting. GLL: design of data capture instrument. JLB, Database maintenance and data retrieval. JO: data cleaning and reference management. BS: statistics. PB: drafting, reference checking. DLC: senior author, general supervision, co-ordination and assistance at all levels.

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# Chapter 3

## Introduction

The first two chapters highlighted the high mortality associated with cerebral GSWs. However, they also demonstrated that there is a subset of patients who may have a reasonable clinical outcome. It is important to identify such patients early so that aggressive treatment can be directed appropriately. On the other hand, it is equally important to identify those with a poor prognosis to avoid wasteful and fruitless expenditure of precious resources in our environment. This is especially important in our developing world setting where resources are much more limited. Numerous prognostic factors have been proposed in the literature but almost all are based on US populations. The only prognostic score specific to the South African context was based on the original work from Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg, but this has never been validated in any other population groups. CHBAH is based in Soweto and serves a population of over 4 million including those on the outskirts of this historically black township. PMTS serves a total catchment population of over 3 million in western KZN who are also predominantly black South Africans. Both institutions are the major academic trauma centres in the respective provinces. In this paper, titled ***'Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: The Pietermaritzburg experience'***, the focus is directed at validating the 'Baragwanath mortality-prediction score' in our similar patient cohort in KZN.

## Key Findings

The Baragwanath mortality-prediction score based on clinically available parameters (admission blood pressure, brain matter spillage and consciousness level) is directly applicable to our patient cohort. It accurately predicted those patients who were unlikely to survive and yielded similar accuracy to the original patient cohort in Johannesburg. This is a highly relevant and potentially valuable tool that should be further validated in other centres across South Africa.

## Publication 3

**Kong VY**, Oosthuizen GV, Sartorious B, Bruce JL, Laing GL, Weale R, Clarke DL. Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: The Pietermaritzburg experience. *Eur J Trauma Emerg Surg*. 2018; 44(4):615-620. DOI: 10.1007/s00068-017-0835-1.

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ORIGINAL ARTICLE

# Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: the Pietermaritzburg experience

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**Abstract**
*Introduction* Cerebral gunshot wounds (GSW) are highly lethal injuries. To date, only one clinical scoring system to predict mortality in a developing world setting has been described. This is the Baragwanath mortality prediction score ("*ABC*": admission blood pressure, brain matter spillage and consciousness level).
*Materials and methods* We performed a retrospective review of prospectively entered data for a cohort of patients with isolated cerebral GSWs over a 5-year period (January 2010–December 2014) in our institution. We aimed to validate the Baragwanath ABC mortality prediction score in our population.
*Results* During the 5-year study period, 102 patients with isolated cerebral GSWs were reviewed, 22% (22/102) of which died. Based on the total ABC score (1–5), the mortality was 0% for 1, 21% for 2, 67% for 3, 92% for 4, and 100% for 5. The ABC score has a sensitivity of 82% (95% CI 60–95%), specificity of 96% (95% CI 89–99%), PPV of 86% (95% CI 66–96%) and NPV of 95% (95% CI 86–99%).
*Conclusions* The Baragwanath mortality prediction score accurately predicts non survival of patients with a cerebral GSW in our patient cohort. Further validation studies in other populations are required before this system can be widely adopted.

**Keywords** Gunshot wounds · Prediction score · Mortality

## Introduction

Cerebral GSWs represent one of the most lethal forms of traumatic brain injury and are associated with a high mortality rate [1]. The literature suggests that over 90% of victims die before arriving at hospital, and a further 50% of these succumb in the resuscitation room [1, 2]. Management of these patients is labour intensive, consumes scarce resources and places a massive burden on already overstretched trauma services, especially in the developing world [4–6]. Numerous prognostic indicators have been reported and most of these emanate from the United States or the military setting [1, 2, 7–9]. However, very little is known regarding their applicability in other settings, especiallying in a developing country such as South Africa, where firearm-related trauma has reached epidemic proportions [6]. Stoffel et al. from Baragwanath Hospital (BH) in Johannesburg published the only South African study to date on this topic. They used a simplified clinical score based on three clinical parameters ("*ABC*": admission blood pressure, brain matter spillage and consciousness level) to aid selection of non-salvageable patients [1]. This proposed scoring system has not been subjected to any formal validation. The aim of this study was to validate the scoring system by applying it to our similar patient cohort.

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## Materials and methods

### Clinical setting

This was a retrospective study undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Our regional electronic trauma registry (HMER©) was reviewed over a 5-year period from January 2010 to December 2014. Ethics approval for this study and for maintenance of the registry was formally endorsed by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu Natal (Reference: BE 207/09). The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of KwaZulu Natal province. It also serves as the trauma referral centre for 19 rural hospitals within the province, with a total catchment population of over three million. Approximately 4000 trauma cases are admitted to the PMTS per annum, with over 50% penetrating trauma. This is a direct reflection of the high incidence of firearm related interpersonal violence and criminal activities experienced throughout the entire province. Baragwanath Hospital (BH) serves a large urban population of Soweto in Johannesburg and is one of the major academic trauma centres in Gauteng province [10].

### The 'Baragwanath ABC score'

The original scoring system proposed by Stoffel et al. utilises three clinical parameters which are readily available in the resuscitation room [1]. These were summarised as the ABC score: admission systolic blood pressure, brain matter spillage visible on inspection, and the patient's level of consciousness on admission. Admission systolic blood pressure (SBP) was subdivided into three distinct categories: (1) <100 mmHg; (2) 100–199 mmHg; and (3) >200 mmHg. Brain matter spillage was subdivided as either 'oozers' and 'non-oozers'. The level of consciousness was arbitrarily categorised based on Glasgow Coma Scale (GCS) into 'conscious' (GCS >6) and 'unconscious' (GCS ≤6). Mortality based on each individual parameter is summarised in Table 1. A mortality prediction score based on a combination of all three parameters is summarised in Table 2.

### The study

All patients treated by the PMTS between January 2010 and December 2014 with an isolated cerebral GSW were included in the study. Those with concurrent GSWs to other body regions were excluded. We categorised our cohort using the Baragwanath ABC score and compared our outcomes with the published data from Stoffel et al.

**Table 1** ABC scoring system

| Admission SBP | Brain spillage | Consciousness | Score |
|---|---|---|---|
| <100 | Non-oozers | Conscious | 1 |
| | | Unconscious | 3 |
| | Oozers | Conscious | 2 |
| | | Unconscious | 4 |
| 100–199 | Non-oozers | Conscious | 0 |
| | | Unconscious | 2 |
| | Oozers | Conscious | 1 |
| | | Unconscious | 3 |
| >200 | Non-oozers | Conscious | 2 |
| | | Unconscious | 4 |
| | Oozers | Conscious | 3 |
| | | Unconscious | 5 |

*SBP* systolic blood pressure

**Table 2** Predicted mortality based on ABC score

| Score | Mortality (%) |
|---|---|
| 0 | 4 |
| 1 | 11 |
| 2 | 22 |
| 3 | 40 |
| 4 | 61 |
| 5 | 78 |

*ABC* admission blood pressure, brain matter spillage and consciousness level

### Statistical analysis

Data were processed and analysed using Stata 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) and statistical package R 3.2.4 [R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org]. Continuous variables were summarised using mean and standard deviation (SD). Association between categorical variables and survival were assessed using the Pearson chi-squared ($\chi^2$) test or Fisher's exact if expected cell count with fewer than observations. A $p$ value less than 0.05 was deemed statistically significant. Several criteria can be applied to identify optimal cut-offs using receiver operating characteristic (ROC) curves. An optimal breakpoint of 2 + ABC score for mortality prediction based on PMTS data was identified using a positive predictive value (PPV) optimization procedure [12]. Diagnostic capability (sensitivity, specificity, PPV and NPV) of this threshold score were estimated along with 95% confidence intervals.

## Results

### The PMTS cohort

During the 5-year study period, a total of 102 patients with isolated cerebral GSWs were identified. Ninety-two percent (94/102) were male and the mean age was 29 years. Ninety-four percent (94/102) of injuries were related to interpersonal violence (assaults) and the remaining 6% (6/102) were attempted suicides. Ninety-eight percent (100/102) involved the use of low velocity firearms (LVF), and the remaining 2% (2/102) were from high velocity firearms (HVF). The mean [standard deviation (SD)] values of physiological parameters on arrival were as follows: heart rate: 85 (24) bpm, systolic blood pressure: 124 (22) mmHg, temperature: 36 °C (1). The mean (SD) GCS on arrival was 12 (5). Thirty percent (31/102) of all patients had visible brain matter (VBM) oozing from the wound. All 102 patients underwent computed tomography scans (CT). Thirty percent (31/102) required neurosurgical interventions. Twenty-eight (90%) of these 31 patients underwent debridement and/or elevation of depressed skull fracture and three required formal craniotomies for haematoma evacuation. Of the 102 patients, 22% (22/102) died during the admission. The remaining 80 patients (78%) survived to discharge and rehabilitation. The mean (SD) GCS on discharge of all 80 survivors was 14 (2). Table 3 summarises the key charateristics of the PMTS cohort.

**Table 3** Characteristics of the PMTS cohort

| Patient characteristics | *N* = 102 |
|---|---|
| Mean age (years) [SD] | 29 [8] |
| Male | 94 [92%] |
| Female | 8 [8%] |
| Mean time to arrival (h) [SD] | 11 [7] |
| Mean systolic pressure (mmHg) [SD] | 124 [22] |
| Mean GCS on arrival [SD] | 12 [5] |
| Visible brain matter oozing | 31 [30%] |
| No visible brain matter oozing | 71 [70%] |
| Computed tomography | 102 [100%] |

*PMTS* Pietermaritzburg Metropolitan Trauma Service, *N* total number, *SD* standard deviation, *GCS* Glasgow coma scale

### Mortality rate

Based on each of the three clinical parameters, the predicted mortality rate for our cohort was as summarised in Tables 4 and 5.

### Mortality prediction score

Table 6 summarises the mortality prediction score applied to our cohort based on all three parameters of the ABC score. Figure 1 shows the trend for predicted mortality of both PMTS and BH cohort based on the ABC score.

An optimal breakpoint of 2 + ABC score for mortality prediction based on PMTS data was identified using a positive predictive value (PPV) optimization procedure. This yielded high sensitivity (82%, 95% CI 60–95%), specificity (96%, 95% CI 89–99%), PPV (86%, 95% CI 66–96%) and NPV (95%, 95% CI 86–99%). The area under curve (AUC) for this cut-off was 0.97 (95% CI 0.94–1.00) which was well above the accepted cut-off of 0.8 for a good predictor. This was shown in Fig. 2.

**Table 4** Predicted mortality for PMTS cohort

| PMTS data | *N* = 102 | Died | % | Survived | % | *p* value |
|---|---|---|---|---|---|---|
| A score | | | | | | |
| SBP < 100 | 10 | 6 | 60 | 4 | 40 | <0.001 |
| SBP 100–199 | 90 | 14 | 16 | 76 | 84 | |
| SBP > 200 | 2 | 2 | 100 | 0 | 0 | |
| | 102 | | | | | |
| B score | | | | | | |
| Non oozers | 71 | 5 | 7 | 66 | 93 | 0.001 |
| Oozers | 31 | 17 | 55 | 14 | 45 | |
| | 102 | | | | | |
| C score | | | | | | |
| GCS > 6 | 83 | 5 | 6 | 78 | 94 | <0.001 |
| GCS ≤ 6 | 19 | 17 | 89 | 2 | 11 | |
| | 102 | | | | | |

*PMTS* Pietermaritzburg Metropolitan Trauma Service, *ABC* admission blood pressure, brain matter spillage and consciousness level, *N* total number, *SBP* systolic blood pressure, *GCS* Glasgow coma scale

**Table 5** Predicted mortality for BH cohort

| BH data | $N=214$ | Died | % | Survived | % | *p* value |
|---|---|---|---|---|---|---|
| A score | | | | | | |
| SBP < 100 | 53 | 20 | 38 | 33 | 62 | 0.003 |
| SBP 100–199 | 143 | 26 | 18 | 117 | 82 | |
| SBP > 200 | 7 | 4 | 57 | 3 | 43 | |
| | 203 | | | | | |
| B score | | | | | | |
| Non oozers | 147 | 29 | 20 | 118 | 80 | <0.001 |
| Oozers | 67 | 29 | 43 | 38 | 57 | |
| | 214 | | | | | |
| B score | | | | | | |
| GCS > 6 | 84 | 7 | 8 | 77 | 92 | <0.001 |
| GCS ≤6 | 130 | 51 | 39 | 79 | 61 | |
| | 214 | | | | | |

*BH* Baragwanath Hospital, *ABC* admission blood pressure, brain matter spillage, *N* total number, *SBP* systolic blood pressure, *GCS* Glasgow coma scale

**Table 6** Comparison between predicted mortality for PMTS and BH cohorts

| ABC score | PMTS mortality | BH mortality (%) | *p* value |
|---|---|---|---|
| 0 | 0% | 4 | 0.002 |
| 1 | 21% | 11 | |
| 2 | 67% | 22 | |
| 3 | 92% | 40 | |
| 4 | 100% | 61 | |
| 5 | N/A | 78 | |

*PMTS* Pietermaritzburg Metropolitan Trauma Service, *BH* Baragwanath Hospital, *ABC* admission blood pressure, brain matter spillage and consciousness level

## Discussion

Cerebral GSWs are associated with significant mortality [4–6]. Historically, the management of these injuries in the civilian setting was extrapolated from experience gained in major military conflicts, the most notable being the Vietnam War [13]. However, over the past three decades, improvements in prehospital care, early aggressive resuscitation, the widespread availability of advanced imaging, coupled with improved neurosurgical techniques have resulted in marked improvements in patient outcomes [2, 3, 14]. Nevertheless, cerebral GSWs remain one of the most lethal forms of traumatic brain injury, with over 90% of patients dying prior

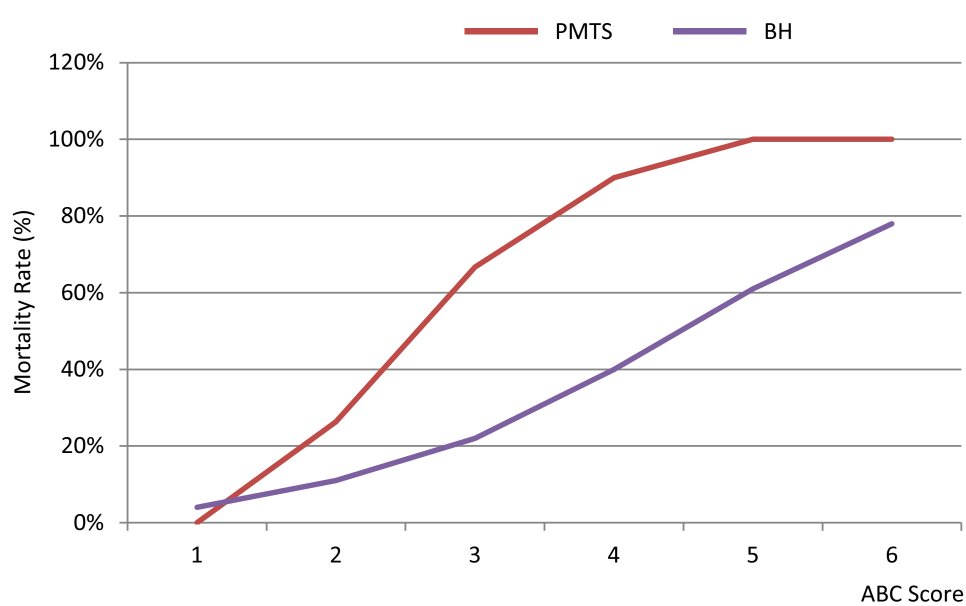


**Fig. 1** Mortality prediction for PMTS and BH (*PMTS* Pietermaritzburg Metropolitan Trauma Service, *BH* Baragwanath Hospital, *ABC* admission blood pressure, brain matter spillage and consciousness level)

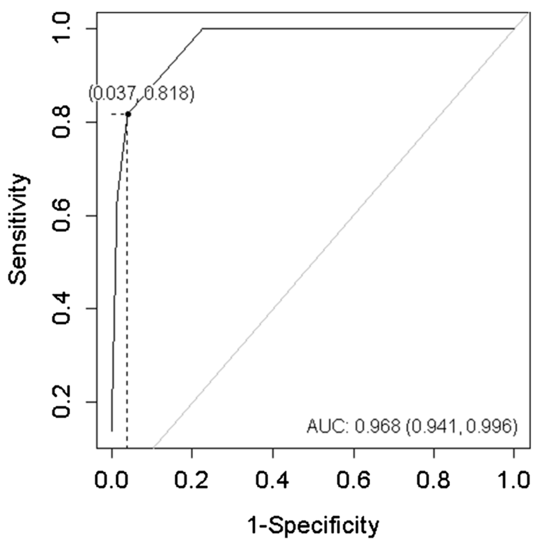


**Fig. 2** AUC mortality prediction based on PMTS data. *AUC* area under the *curve, PMTS* Pietermaritzburg Metropolitan Trauma Service

to reaching hospital. Of those who reach hospital alive, a further 50% will succumb in the resuscitation room [2, 3].

Given the lethality of these injuries, clinicians are often faced with difficult decisions surrounding the issue of futility and the appropriate alloction of scarce resources [4]. This is especially relevant in developing countries such as South Africa, where the resources to manage the trauma epidemic are perennially insufficient [5]. Numerous studies have proposed a multitude of risk factors which predict a poor prognosis and mortality [2, 3, 7–9]. A study by Aldrich et al. found that GCS on admission is the strongest predictor of mortality [15]. The majority of American neurosurgeons regard the subgroup of patients with a low initial GCS score as having a very poor prognosis and tend to withhold aggressive treatment in these patients. However, some authors have also reported good outcomes in patients with an initial GCS less than 5 [1, 15].

At present, literature from the developing world is limited. The only two studies to date were by Stoffel et al. from Baragwanath Hospital which is a public institution [1], and Glapa et al. from Milpark Hospital which is a private institution [16], both of which are in Johannesburg. Stoffel et al. reported an overall mortality of 27% [1], while mortality from the study by Glapa et al. was 58% [16]. Stoffel et al. proposed a simple clinical scoring system and pointed out that many studies from the developed world place heavy emphasis on predictive factors which are not immediately available to clinicians during the initial phase of resuscitation in the trauma room. These include patient risk factors, laboratory results, specific computed tomography findings, and post resuscitation GCS. In his series of 214 patients, a combined score of five based on their algorithm was associated with a mortality rate of 80%. In our present study, we have shown that by applying this scoring system to our similar patient cohort, it accurately predicts mortality. To our knowledge, ours is the only study to date that attempted to validate this score. A score of 5 in our setting is associated with 100% mortality. This observed difference may be related to slight geographical variation and different prehospital emergency medical service (EMS) network, transfer time and management protocol [17].

Born out of necessity, the surgical philosophy of selective conservatism has been at the core of trauma care in South Africa for over half a century [5]. The early identification of those with a dismal prognosis is crucially important and has significant implication on decision making by clinicians in the resuscitation room. The corollary is that those who survive to reach our institution and who have a reasonable chance of survival must not be denied treatment based exclusively on mechanism or a single factor such as low GCS. A simple multi-parameter clinical scoring system may allow objective identification of those patients who are potentially unsalvageable in a resource constrained environment. This simplified scoring system may also be applicable to other settings with high incidence of cerebral GSWs, but further validations in other centres outside South Africa are required.

## Conclusions

Cerebral GSWs are highly lethal. The Baragwanath mortality prediction score is directly applicable and valid in our local setting. It accurately predicts those patients who were unsalvageable. Further validation studies in other populations are required before this scoring system can be more widely adopted.

**Compliance with ethical standards**

**Conflict of interest** Authors declare that they have no conflict of interest.

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# Chapter 4

## Introduction

In Chapter 3, the 'Baragwanath mortality-prediction score' based on the original work from CHBAH in Johannesburg was validated and found to be directly applicable to our patient cohort with cerebral GSWs in KZN. Although it is accurate, each clinical parameter (admission blood pressure, brain matter spillage and consciousness level) requires a separate value assigned and enumeration of the total score that correlates with mortality which is somewhat cumbersome thus potentially limiting its use in the resuscitation room setting. In this paper, titled ***'Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: The Maritzburg Score'***, our patient cohort was further analysed and a simplified clinical score was proposed based on parameters that were readily available during the initial resuscitation of patients on admission. The proposed clinical score was designed on the premise that most predictive prognostic factors should also be easy to identify and practical in value. This clinical score was named the 'Maritzburg Score' as a tribute to original work based in Pietermaritzburg, often affectionately known as 'Maritzburg'.

## Key Findings

By using only the two most easily available clinical variables, namely the presence of visible brain matter and a GCS motor score < 5, our simplified score accurately predicts non-survivors of cerebral GSWs. The strength of the 'Maritzburg Score' lies in its simplicity and it appears to perform as well as the 'Baragwanath mortality-prediction score'. This new score should be validated in other patient cohorts.

## Publication 4

**Kong VY**, Clarke DL, Oosthuizen GV, Esterhuizen T, Bruce JL, Laing GL, Odendaal JJ. Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: The Maritzburg Score. *Ann R Coll Surg Engl*. 2018; 100(2):97-100. DOI: 10.1308/rcsann.2017.0141.

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# Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: The Maritzburg Score

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**ABSTRACT**

INTRODUCTION Cerebral gunshot wounds are highly lethal and literature on the clinical scores for mortality prediction is limited.

MATERIALS AND METHODS A retrospective study was undertaken over a 5-year period at the Pietermaritzburg Metropolitan Trauma Service in South Africa. A simplified clinical prediction score was developed based on clinical and/or physiological variables readily available in the resuscitation room.

RESULTS A total of 102 patients were included; 92% (94/102) were male and the mean age was 29 years; 22% (22/102) died during the admission. The presence of visible brain matter (odds ratio 12.4, $P = 0.003$) and motor score less than 5 (odds ratio 89.6, $P < 0.001$) allows the prediction success of 92% (sensitivity 73% and specificity 98%). The area under the receiver operating characteristic curve was 94% (95% confidence interval 88–100%, $P < 0.001$).

CONCLUSIONS The presence of visible brain matter, together with a motor score of less than 5, allows accurate identification of non-survivors of cerebral gunshot wounds. Further study is required to validate this score.

**KEYWORDS**
Cerebral – Gunshot wound – Mortality

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## Introduction

Cerebral gunshot wounds are the most lethal form of traumatic brain injury and are associated with a high mortality.[1] The management of patients with such injury is resource intensive and places a substantial burden on the already overstretched trauma services in South Africa. This often raises difficult questions regarding the appropriate allocation of precious resources.[2,3] An effective clinical triage tool that allows early and reliable identification of non-survivors assists clinicians in directing resources appropriately and avoids potentially futile care. Stoffel et al., from Baragwanath Hospital in Johannesburg, proposed a scoring system which uses three clinical parameters (admission blood pressure, brain matter spillage and summed Glasgow Coma Scale) and has been validated.[1] Glasgow Coma Scale (GCS) comprises three separate components: eye opening, verbal and motor response. Recent literature suggested that the motor component of GCS performs as well as the summed GCS in predicting mortality of patients with traumatic brain injury.[4] Furthermore, eye opening and verbal response may be difficult to assess accurately in the resuscitation room, where patients are often intoxicated and may have other confounding factors, such as facial swelling. In light of this, we designed our current study to propose a more simplified clinical score that would allow early prediction of mortality in patients with isolated cerebral gunshot wounds.

## Materials and Methods

### Clinical setting

A retrospective study was undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Our electronic regional trauma registry was reviewed over a 5-year period from January 2010 to December 2014. Ethics approval for this study and for maintenance of the registry was formally endorsed by the Biomedical Research Ethics Committee of the University of

KwaZulu Natal (reference: BE 207/09). The PMTS provides definitive trauma care to the city of Pietermaritzburg (often referred to as 'Maritzburg'), the capital of KwaZulu Natal province. It also serves as the trauma referral centre for 19 other rural hospitals within the province, with a total catchment population of over three million. Although the PMTS is located in the capital city of the province, the sole provincial neurosurgery centre is based at Inkosi Albert Luthuli Central Hospital in Durban, so all cases who require neurosurgical intervention are transferred out from PMTS. Approximately 3000 trauma cases are admitted to the PMTS per annum, with over 50% being penetrating traumas. This is a direct reflection of the high incidence of firearm-related interpersonal violence and criminal activities experienced throughout the entire province.

### The study

All patients with a single, isolated cerebral gunshot wound were included. Those with concurrent gunshot wounds to other body regions were excluded. Basic demographic data were reviewed. Further data reviewed included the mode of injury (assault, suicide or accident), type of firearms, vital signs (physiological parameters on arrival), physical examination findings, GCS and the final clinical outcome. The GCS was further divided into its component scores of eye opening, vocal response and motor response for each patient.

### Statistical analysis

The IBM SPSS version 23 statistical program was used to analyse the data. Crude associations between independent variables and the outcome of death or survival were assessed using Pearson's chi square test or Fisher's exact tests, as appropriate, in the case of categorical variables. Continuous variables were tested using t-tests or Mann-Whitney nonparametric tests, as appropriate. Receiver operating characteristic analysis was used to determine the optimum cut-off points for each variable to predict mortality. Multiple logistic regressions were used to determine predictors independently and significantly associated with mortality and to determine a simple clinical model to predict mortality with a high level of accuracy. A backward stepwise model was used with entry and exit probabilities set at 0.05 and 0.1, respectively.

## Results

### Patient cohort

During the 5-year study period, a total of 102 patients with isolated cerebral gunshot wounds were included; 92% (94/102) were male and the mean age was 29 years; 94% (94/102) of injuries were related to interpersonal violence (assaults) and the remaining 6% (6/102) were attempted suicides. The mean and standard deviation (SD) values of physiological parameters on arrival were heart rate 85 beats/minute (SD 24 beats/minute), systolic blood pressure 124 mmHg (SD 22 mmHg), temperature 36°C.[1] The mean GCS on arrival was 12 (SD 5) and 33% (31/102) of all patients had visible brain matter oozing from the wound. All 102 patients underwent computed tomography (CT). Of the 102 patients, 22% (22/102) died during admission. The remaining 80 patients (78%) survived until discharge to rehabilitation. The mean GCS on discharge of all 80 survivors was 14 (SD 2).

**Table 1** Comparison of demographics and clinical parameters of non-survivors and survivors of cerebral gunshot wounds

| | **Non-survivors (*N* = 22)** | | **Survivors (*N* = 80)** | | ***P* value** |
|---|---|---|---|---|---|
| *Demographic:* | **Mean** | **SD** | **Mean** | **SD** | |
| Age | 30 | 10 | 29 | 8 | 0.7943 |
| Male | 22 | 100% | 72 | 90% | 0.196 |
| Female | 0 | 0% | 8 | 10% | |
| *Clinical parameters:* | | | | | |
| Respiratory rate (minute) | 17 | 6 | 18 | 4 | 0.3915 |
| Heart rate (minute) | 76 | 30 | 87 | 21 | 0.0336 |
| Systolic blood pressure (mmHg) | 124 | 29 | 124 | 19 | 0.608 |
| Temperature (°C) | 36 | 1 | 37 | 1 | 0.0012 |
| Visible brain matter | 17 | 77% | 14 | 18% | < 0.001 |
| No visible brain matter | 5 | 23% | 66 | 83% | |
| Admission Glasgow Coma Scale | 4 | 3 | 14 | 2 | < 0.001 |
| Eye-opening component (median, IQR) | 1 | (1–2) | 4 | (4–4) | < 0.001 |
| Vocal response component (median, IQR) | 1 | (1–1) | 5 | (4–5) | < 0.001 |
| Motor response component (median, IQR) | 2 | (1–5 ) | 6 | 6–6 | < 0.001 |

**Table 2** Comparison between non-survivors versus survivors in terms of the need for neurosurgical intervention

| | Non-survivors ($N$ = 22) | | Survivors ($N$ = 80) | | $P$ value |
|---|---|---|---|---|---|
| | ($n$) | (%) | ($n$) | (%) | |
| Neurosurgical intervention | 6 | 27 | 25 | 31 | 0.799 |
| No neurosurgical intervention | 16 | 73 | 55 | 69 | 0.799 |

### Non-survivors compared with survivors

Direct comparison was made between the 22 non-survivors and the 80 survivors. Table 1 summarises this comparison in terms of demographics and clinical parameters.

### Neurosurgical interventions

Some 30% (31/102) of all patients required neurosurgical interventions; 28 (90%) of these 31 patients underwent debridement and/or elevation of depressed skull fracture and 3 required formal craniotomy for haematoma evacuation. There was no significant difference in outcome between non-survivors and survivors in terms of the need for neurosurgical interventions (27% vs. 31%, $P = 0.799$). This is summarised in Table 2.

### Clinical prediction model

To derive a clinically relevant model of practical value, the following parameters were entered into a backward stepwise model: clinical and/or physiological variables on admission (temperature, heart rate, systolic blood pressure, motor score and the presence of visible brain matter) were considered in succession. Using backward selection, after four steps, the following two factors remained as the best predictors in the model: visible brain matter (odds ratio, OR, 12.4, $P = 0.003$) and motor score less than 5 (OR 89.6, $P < 0.001$). The prediction success for this model was 92% (sensitivity 73%, specificity 98%). The area under the receiver operating characteristic curve (AUROC) was 94% (95% confidence interval, CI, 88–100%, $P < 0.001$). The ROC curve for the combined model is shown in Figure 1. The model coefficients were highly statistically significant against the constant-only model (chi square 61.4, $P < 0.001$; Nagelkerke's R squared 0.699 indicated a high level of variance explained by the model).

## Discussion

Cerebral gunshot wounds are associated with significant mortality.[1,5–8] Historically, the management of these injuries in the civilian setting has relied heavily on the published experience from the Vietnam war.[9] Over the past three decades, major improvements in pre-hospital care and changes in resuscitation strategies, together with almost universal availability of advanced imaging, coupled with parallel development in neurosurgical techniques have resulted in marked improvements in patient outcomes.[5,6,10] However, over 90% of victims still die before reaching hospital and a further 50% die in the resuscitation room.[5–10]

Given the dismal prognosis for many patients, clinicians are often faced with difficult decisions as to the subgroup which may benefit from intensive management.[11] Numerous studies have proposed a multitude of risk factors for predicting poor prognosis.[5–14] These include an admission GCS less than 5, unilateral or bilateral large or unreactive pupils, subarachnoid haemorrhage, intra-cerebral haematoma, ventricular injury on CT, missile traversing the central part of the brain, diffuse fragmentation, hypoxia, prolonged extraction times, self-harm, high velocity injury, deranged coagulation and advanced age.[5–14] Many of these are not immediately known or available to the clinicians in the resuscitation room.[1]

A study by Aldrich et al.[15] found that initial GCS on admission is the strongest predictor of mortality. The majority of neurosurgeons regard the patient subgroup with a low initial GCS scores as being ultimately unsalvageable and tend to limit aggressive treatment.[1,15] On the other hand, good outcomes for patients with a low initial GCS have been also reported.[1,15] The only two South African studies to date were both from Johannesburg.[1,16] The original score proposed by Stoffel et al.[1] was based on his series of 214 patients using three clinical parameters. Admission systolic blood pressure was divided into three further categories (< 100 mmHg, 100–199 mmHg and ≥ 200 mmHg). The presence of visible brain matter was dichotomised (present or absent) and the summed GCS was arbitrarily defined as either ≤ 6 or > 6. Each variable was assigned a different value and combined score of 5 based on this algorithm is associated with 80% mortality. The complex algorithm places limitation on the usefulness of such score and thus a more simplified clinical score is preferable.

In our experience, accurate assessment of each component of the GCS in the setting of cerebral gunshot wounds is often challenging, especially with concurrent facial swelling and often intoxicated patients. The use of motor score alone has been shown to be as accurate as the summed GCS in traumatic brain injury.[4] In our present model, we propose the 'Maritzburg score'; by using only two simple clinical variables: the presence of visible brain matter and a motor score less than 5 allows accurate identification of non-survivors.

Selective conservatism has been the underlying philosophy behind trauma care in South Africa for over half a century.[3] Correct and early identification of those with a dismal prognosis is important. On the other hand, those who survive to reach our institutions must not be denied treatment based on anecdotal evidence and any single clinical factor. By applying a simple two-parameter clinical scoring system to these injuries, it is possible to objectively identify those patients who are unsalvageable. This may allow for the more rational allocation of scarce resources in a resource constrained environment.

## Conclusions

By using two simple clinical variables, namely the presence of visible brain matter and a motor score of less than 5, our clinical prediction score allows accurate identification of non-survivors of cerebral gunshot wounds. Further study is required to validate this score.

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# Chapter 5

## Introduction

The previous two chapters highlighted the utility and relevance of clinical-prediction scores for mortality in patients with cerebral GSWs. Serum lactate level is frequently measured in trauma patients as part of initial management in the resuscitation room. Although its role in prognostication and guidance of resuscitation, especially in torso trauma has long been appreciated, its exact role in the context of isolated traumatic brain injury (TBI) remains highly controversial. While an elevated serum-lactate level in trauma is considered a surrogate for cellular derangement with anaerobic metabolism and associated with adverse outcome, there is little agreement on whether this is applicable to TBI. The few studies that are available are mostly based on animal models and there has been no study to date that examined the role of serum lactate level specifically in the context of cerebral GSW. This paper, titled ***‘A raised serum-lactate level is an independent predictor of in-hospital mortality in patients with isolated cerebral gunshot wounds’***, focuses specifically on the relationship between elevated serum-lactate levels and in-hospital mortality in patients with isolated cerebral GSWs.

## Key Findings

Serum lactate level on admission appeared to correlate with the severity of TBI in the context of cerebral GSW. Higher levels are associated with more severe injury (lower GCS). A raised serum-lactate level is closely correlated with in-hospital mortality.

## Publication 5

**Kong VY**, Weale R, Sartorius B, Oosthuizen GV, Bruce JL, Laing GL, Clarke DL. A raised serum-lactate level is an independent predictor of in-hospital mortality in-patients with isolated cerebral gunshot wounds. *S Afr Med J*. 2018; 108(5):413-417. DOI: 10.7196/SAMJ.2018.v108i5.12837.

# A raised serum lactate level is an independent predictor of in-hospital mortality in patients with isolated cerebral gunshot wounds

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**Background.** Cerebral gunshot wounds (CGSWs) represent a highly lethal form of traumatic brain injury, and triaging these patients is difficult. The prognostic significance of the serum lactate level in the setting of CGSWs is largely unknown.
**Objectives.** To examine the relationship between elevated serum lactate levels and mortality in patients with isolated CGSWs.
**Methods.** A retrospective review of the regional trauma registry was undertaken at the Pietermaritzburg Metropolitan Trauma Service, South Africa, over a 5-year period from 1 January 2010 to 31 December 2014. All patients with an isolated CGSW were included.
**Results.** A total of 102 patients with isolated CGSWs were identified. Of these, 92.2% (94/102) were male. The mean age (standard deviation) was 29 (8) years, and the in-hospital mortality rate was 21.6% (22/102). The mean serum lactate level was significantly higher among non-survivors than among survivors (6.1 mmol/L v. 1.3 mmol/L; $p<0.001$). Lactate levels among non-survivors were <2 mmol/L in 4.5%, 2 - 3.99 mmol/L in 9.1%, 4 - 5.99 mmol/L in 36.4% and ≥6 mmol/L in 50.0%. The odds ratio for mortality with a lactate level of 4 - 5.99 mmol/L was 67 (95% confidence interval (CI) 1.7 - 2 674.2), while for a lactate level of ≥6 mmol/L it was 1 787 (95% CI 9.0 - 354 116.1). The serum lactate level accurately predicted mortality even after adjustment for other variables. Based on a receiver operating curve analysis, an optimal cut-off of 3.3 mmol/L for serum lactate as a predictor for mortality was identified (area under the curve = 0.957).
**Conclusions.** CGSWs are associated with significant mortality, and a raised serum lactate level appears to be an independent predictor of in-hospital mortality. It is a potentially useful adjunct in the resuscitation room for identifying patients with a very poor prognosis.

*S Afr Med J* 2018;108(5):413-417. DOI:10.7196/SAMJ.2018.v108i5.12837

Cerebral gunshot wounds (CGSWs) are a highly lethal form of traumatic brain injury (TBI), yet there are patients who survive these devastating injuries.[1-3] Triaging these patients is difficult, and accurate early prognostic indicators may help clinicians to make appropriate decisions.[1-5] The prognostic significance of a raised serum lactate level in torso trauma has long been appreciated. In this setting, it is able to guide resuscitation and to a certain extent predict clinical outcome.[6,7] However, the role of lactate in the context of an isolated TBI remains controversial [8-13]. Some authors have suggested that elevated serum lactate levels do not correlate with the extent of the cerebral cellular metabolic derangement in these patients, and that the predictive value of serum lactate in TBI is poor.[8-10]

Others, however, have shown that the serum lactate level correlates with the severity of TBI.[11,13]. Some have proposed that a raised serum lactate level is associated with improved neurological outcomes and lower mortality rates in patients with TBI. It has even been suggested that elevations in serum lactate due to anaerobic metabolism in trauma patients may in fact be neuroprotective.[8]

## Objectives

To interrogate the relationship between serum lactate levels and mortality in patients with isolated CGSWs in order to improve prediction of mortality in these patients.

## Methods

### Clinical setting

This was a retrospective study undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS) in Pietermaritzburg, South Africa (SA). Our electronic regional trauma registry was reviewed for the 5-year period from 1 January 2010 to 31 December 2014. Ethics approval for this study and for maintenance of the registry was granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. no. BE 207/09 BCA 221/13). The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of KwaZulu-Natal Province. It is one of the largest academic trauma centres in the province and serves as the referral centre for 19 other hospitals in the province, with a total catchment population of over 3 million. Approximately 4 000 trauma cases are admitted to the PMTS per annum, with over 50% being due to penetrating trauma. This is a direct reflection of the high incidence of firearm-related interpersonal violence and criminal activities throughout the entire province.

### Criteria

All patients with single isolated CGSWs were included in the study. Those with concurrent gunshot wounds to other body regions (neck, chest, etc.) were excluded. All patients were managed in accordance with Advanced Trauma Life Support (ATLS) principles. Every patient who has sustained a CGSW has a serum lactate level measurement performed as soon as practical after their arrival in the trauma resuscitation room.

### Assessment

Basic demographic data, vital signs on arrival, physical examination findings, Glasgow Coma Score (GCS) and the final clinical outcome were reviewed. In accordance with ATLS, the conventional severity of TBI grading based on the GCS was used: mild (13 - 15), moderate (9 - 12) and severe (3 - 8). The serum lactate levels were arbitrarily divided into four categories, 0 - 1.99 mmol/L, 2 - 3.99 mmol/L, 4 - 5.99 mmol/L and ≥6 mmol/L, for the purposes of comparison.

### Statistical analysis

The data were processed and analysed using Stata 13.0 (StataCorp, USA). Any associations between admission GCS category, serum lactate and categorical explanatory variables were assessed using Pearson's $\chi^2$ test, or Fisher's exact test if an expected cell count was fewer than 5 observations. Comparison of means of continuous markers by GCS admission category was assessed using one-way analysis of variance. Correlations between GCS admission score and serum lactate were assessed using Spearman's rank correlation coefficient.

## Results

### Description of the patient cohort

During the 5-year study period, 102 patients with isolated CGSWs were treated at our institution. Of these, 92.2% (94/102) were male and the mean (standard deviation (SD)) age was 29 (8) years. Most of the injuries (92.3%, 94/102) were related to interpersonal violence (assault). The remaining 7.8% (8/102) were attempted suicides; all these patients were male. The mean (SD) values of physiological parameters on arrival were as follows: heart rate 85 (24)/min, systolic blood pressure 124 (22) mmHg, temperature 36 (1)°C. The mean (SD) GCS on arrival was 12 (5). Thirty percent (31/102) of all patients had visible brain matter oozing from the wound. All 102 patients underwent computed tomography (CT) scans, of which 21.6% (22/102) revealed a bullet *in situ*. Neurosurgical intervention was required in 30.4% of cases (31/102); 28 (90.3%) of these 31 patients underwent debridement and/or elevation of a depressed skull fracture, and 3 required formal craniotomy for evacuation of a haematoma. Of the 102 patients, 21.6% (22/102) died during the admission. The remaining 80 patients (78.4%) survived to discharge. The mean (SD) GCS on discharge of all 80 survivors was 14.

### CGCS v. lactate levels

Of the 102 patients, 19.6% (20/102) had a GCS of 3 - 8 on admission, 19.6% (20/102) a GCS of 9 - 12 and 60.8% (62/102) a GCS of 12 - 15. Table 1 summarises the demographics, clinical parameters and mean serum lactate level for each of these three severity groups. There was a significant difference in mean lactate level between the three groups, the level increasing as severity as determined by the GCS increased (mild: lactate 1.1 mmol/L, moderate: lactate 2.6 mmol/L, severe: lactate 5.6 mmol/L; $p<0.001$). This is shown in Table 2. A strong

**Table 1. Comparison between mild, moderate and severe injury as determined by the GCS**

| | Mild: GCS 13 - 15 (*N*=62) | Moderate: GCS 9 - 12 (*N*=20) | Severe: GCS 3 - 8 (*N*=20) | *p*-value† |
|---|---|---|---|---|
| Demographics | | | | |
| Age (years), mean (SD) | 29 (8) | 30 (7) | 30 (9) | 0.922 |
| Gender, *n* | | | | 0.284 |
| Male | 55 | 19 | 20 | |
| Female | 7 | 1 | 0 | |
| Clinical parameters | | | | |
| Respiratory rate (per min), mean (SD) | 18 (4) | 19 (4) | 17 (6) | 0.501 |
| Heart rate (bpm), mean (SD) | 89 (21) | 80 (18) | 82 (33) | 0.496 |
| Systolic blood pressure (mmHg), mean (SD) | 125 (20) | 119 (18) | 125 (27) | 0.674 |
| Temperature (°C), mean (SD) | 37 (1) | 36 (1) | 36 (1) | <0.001* |
| Visible brain matter, *n* | | | | <0.001* |
| Yes | 6 | 7 | 18 | |
| No | 59 | 7 | 5 | |
| Laboratory parameter | | | | |
| Serum lactate (mmol/L), mean (SD) | 1.0 (1.1) | 3.3 (2.7) | 5.2 (2.9) | <0.001* |

GCS = Glasgow Coma Score; SD = standard deviation; bpm = beats per minute.
*Statistically significant ($p<0.05$).
†One-way analysis of variance for comparison of means by GCS group; Pearson's $\chi^2$ test or Fisher's exact test (if expected cell count with fewer than 5 observations) used to test association between categorical variables and GCS category.

**Table 2. The four categories of serum lactate levels in relation to GCS**

| Lactate level (mmol/L) | Mild: GCS 13 - 15 (*N*=62), *n* (%) | Moderate: GCS 9 - 12 (*N*=20), *n* (%) | Severe: GCS 3 - 8 (*N*=20), *n* (%) | *p*-value† |
|---|---|---|---|---|
| 0 - 1.99 | 54 (87.1) | 10 (50.0) | 2 (10.0) | <0.001* |
| 2 - 3.99 | 4 (6.5) | 5(25.0) | 3 (15.0) | |
| 4 - 5.99 | 3 (4.8) | 3 (15.0) | 5 (25.0) | |
| ≥6 | 1 (1.6) | 2 (10.0) | 10 (50.0) | |

GCS = Glasgow Coma Score.
*Statistically significant ($p<0.05$).
†Fisher's exact test.

inverse (negative) correlation was noted between serum lactate and admission GCS. The mean serum lactate level among non-survivors was significantly higher than that among survivors (6.1 mmol/L v. 1.3 mmol/L; $p<0.001$) (Fig. 1).

### Serum lactate levels and mortality

There was a direct correlation between increasing serum lactate levels and mortality. Table 3 summarises the differences in demographics, clinical parameters and serum lactate levels between survivors and non-survivors. This relationship is represented graphically in Figs 2 and 3. Both graphs demonstrate a direct relationship between increasing serum lactate levels and increasing mortality. An optimal breakpoint for serum lactate of 3.3 mmol/L for mortality prediction was identified using a positive predictive value (PPV) optimisation procedure for the receiver operating characteristic (ROC) curve (Fig. 4). The area under the curve for this cut-off was 0.957 (95% CI 0.913 - 1.001), which is well above the accepted cut-off of 0.8 for a good predictor. This optimal breakpoint yielded a high sensitivity (95%, 95% CI 77 - 99), specificity (94%, 95% CI 86 - 98), PPV (81%, 95% CI 63 - 99) and negative predictive value (99%, 95% CI 92 - 99). A direct comparison was made between survivors (80/102) and non-survivors (22/102). Table 4 shows how mortality increased with increasing serum lactate levels.

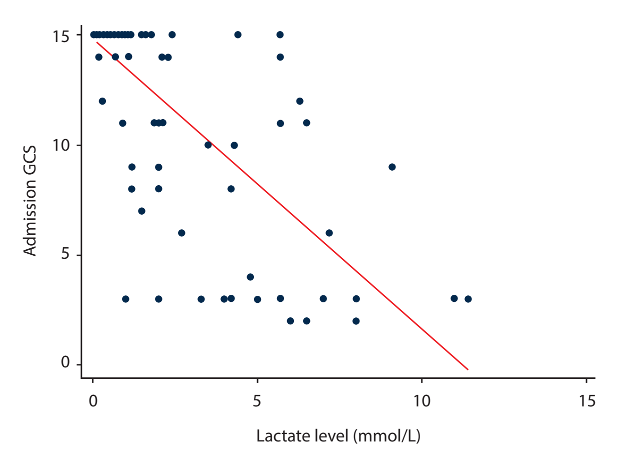


*Fig. 1. Inverse correlation between serum lactate level and admission GCS. (GCS = Glasgow Coma Score.)*

## Discussion

CGSWs are a highly lethal form of TBI, and the severity of the injury strongly determines the outcome. The GCS is a highly successful and tried-and-tested clinical scoring system for blunt TBI. It is simple, elegant and repeatable, and separates TBI into the three broad categories of mild, moderate and severe. Although an elevated serum lactate level is a well-recognised marker of severity in torso trauma, its significance in TBI is unclear.[6-12] Our data suggested a close correlation between increased serum lactate levels and lower GCS. In addition, both these scoring systems correlate with increasing mortality.

Lactate is a waste product of anaerobic metabolism and reflects cellular disruption secondary to hypoperfusion and shock. It is a

**Table 3. Baseline comparison between non-survivors and survivors**

| | Non-survivors (*N*=22) | Survivors (*N*=80) | *p*-value |
|---|---|---|---|
| Demographics | | | |
| Age (years), mean (SD) | 30 (10) | 29 (8) | 0.7943 |
| Gender, *n* (%) | | | 0.196 |
| Male | 22 (100.0) | 72 (90.0) | |
| Female | 0 (0) | 8 (10.0) | |
| Clinical parameters, mean (SD) | | | |
| Respiratory rate (per min) | 17 (6) | 18 (4) | 0.3915 |
| Heart rate (bpm) | 76 (30) | 87 (21) | 0.0336* |
| Systolic blood pressure (mmHg) | 124 (29) | 124 (19) | 0.608 |
| Temperature (°C) | 36 (1) | 37 (1) | 0.0012* |
| Visible brain matter | | | <0.001* |
| Yes | 17 (77.3) | 14 (17.5) | |
| No | 5 (22.7) | 66 (82.5) | |
| Admission GCS | 4 (3) | 14 (2) | <0.001* |
| Laboratory parameter, mean (SD) | | | |
| Serum lactate (mmol/L) | 6.1 (2.5) | 1.3 (1.3) | <0.001* |

SD = standard deviation; bpm = beats per minute; GCS = Glasgow Coma Score.
*Statistically significant ($p<0.05$).

**Table 4. Mortality according to serum lactate level**

| Lactate level (mmol/L) | Non-survivors (*N*=22), *n* (%) | Survivors (*N*=80), *n* (%) | OR (95% CI)† | *p*-value† |
|---|---|---|---|---|
| <2 | 1 (4.5) | 65 (81.3) | 1 (ref) | - |
| 2 - 3.99 | 2 (9.1) | 10 (12.5) | 1.2 (0 - 84) | 0.931 |
| 4 - 5.99 | 8 (36.4) | 4 (5.0) | 66.8 (1.7 - 2 674.2) | 0.026* |
| ≥6 | 11 (50.0) | 1 (1.3) | 1 786.9 (9.0 - 354 116.1) | 0.006* |

OR = odds ratio; CI = confidence interval; GCS = Glasgow Coma Score.
*Statistically significant ($p<0.05$).
†Adjusted for age, heart rate, systolic blood pressure, temperature, visibility of brain matter and low admission GCS (≤8).

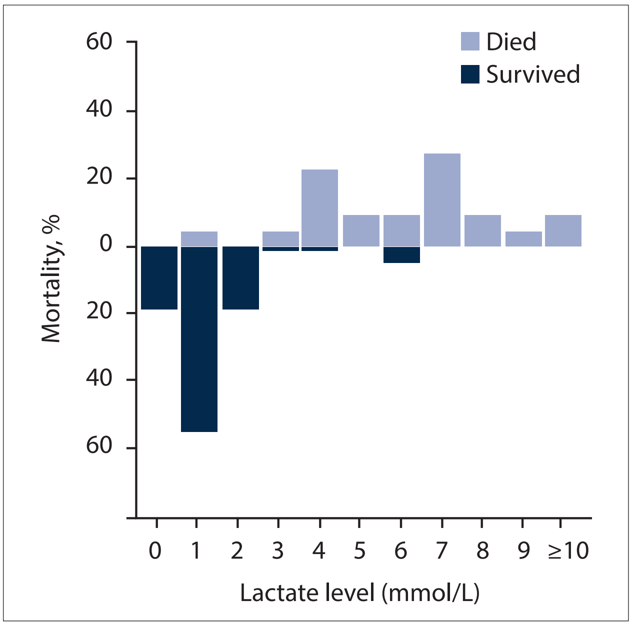


*Fig. 2. Correlation between serum lactate level and mortality.*

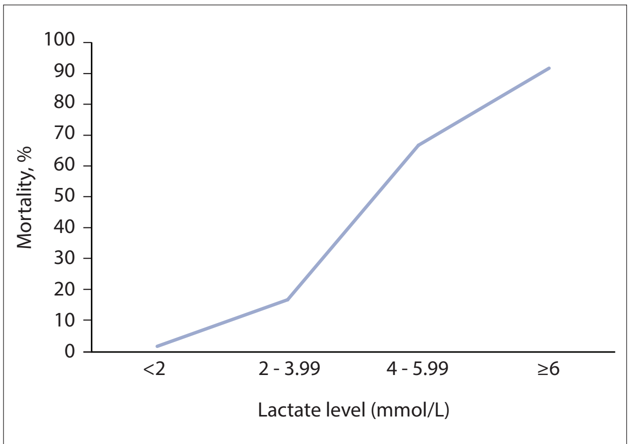


*Fig. 3. Mortality rate according to increasing lactate level category.*

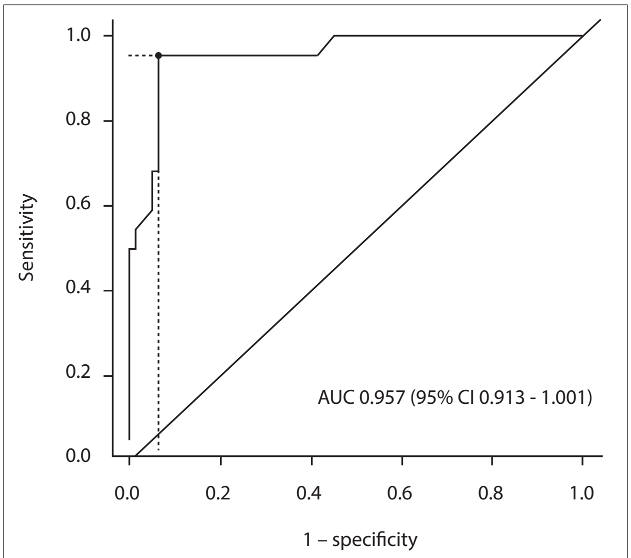


*Fig. 4. ROC curve (criterion: ROC01) for optimal breakpoint identification of serum lactate level for mortality prediction. (ROC = receiver operating characteristic; AUC = area under the curve.)*

better marker of shock states than vital signs, which may only become deranged late in the development of such a state.[6,7] In the context of TBI, some authors have suggested that elevated serum lactate levels reflect a general state of global hypoperfusion rather than cerebral metabolic derangement *per se*.[8-10] In a large series of 555 consecutive cases of isolated TBI, Cureton *et al.*[8] demonstrated that the serum lactate level was closely correlated with severity of TBI. However, they noted that a raised serum lactate level was associated with improved neurological outcomes and lower mortality rates. They went so far as to suggest that elevations in lactate due to anaerobic metabolism in trauma patients may be neuroprotective. Experimental data support this suggestion.[11-13]

The only study on the relationship between TBI and serum lactate in SA to date was from Milpark Hospital in Johannesburg.[5] In this study of 72 consecutive cases of isolated CGSWs, it was noted that the mean lactate level was higher in non-survivors than survivors (6.7 v. 2.7 mmol/L). In the present study, we have demonstrated that elevated serum lactate levels are predictive of increased in-hospital mortality. Using 3.3 mmol/L as a cut-off value, the odds of mortality are well over 300. We have also demonstrated that mortality increases dramatically as the serum lactate level rises. This remains significant even after adjusting for other variables and appears to be an independent predictor of in-hospital mortality. We consider that measurement of serum lactate levels in patients with a CGSW may potentially be useful as a predictor of mortality, especially if used in conjunction with other clinical features such as the GCS and the presence of exposed brain tissue. However, our sample sizes were small and the results should be interpreted with caution.

## Conclusions

CGSWs are associated with significant mortality and a raised serum lactate level appears to be an independent predictor of in-hospital mortality. Serum lactate levels are closely correlated with the severity of penetrating TBI following a CGSW as determined by the GCS. There is an inverse relationship between admission GCS and serum lactate level. Serum lactate levels may well be a useful adjunct in determining the severity of TBI post CGSW. Further studies are required to assess the long-term neuropsychological outcomes in this injury subset in relation to our findings.

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**Author contributions.** VYK: data collection, statistics and writing of article; GLL, JLB, GVO, RDW, BS, PB and DLC: writing of article and production of tables.

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**Conflicts of interest.** None.

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# Chapter 6

### Introduction

This final paper, titled ***'Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: a South African experience'***, examines a simple clinical dilemma of whether or not it is necessary for patients who have sustained an isolated cerebral GSW to be immobilised with a cervical collar. Over the last 40 years, it has become a dogma that all trauma patients must have their cervical spine immobilised until a cervical spine injury has been adequately excluded. This is traditionally achieved by the application of a rigid cervical spine collar to prevent movement of the spine. Recently, there has been concern expressed that this is unnecessary in many cases and may even be potentially harmful. From a clinical standpoint, the rigid collar often causes difficulty in airway management and may decrease cerebral venous drainage thereby potentially exacerbating secondary brain injury.

### Key Findings

The incidence of cervical spine injury following true, isolated cerebral GSW is non-existent. The widely held dogma of routine cervical spine immobilisation, extrapolated to the specific context of isolated cerebral GSW is unfounded and has no evidence base. This practice should be discouraged and resuscitative efforts should instead be directed at preventing secondary brain injury.

**Publication 6**

**Kong VY**, Weale R, Sartorius B, Bruce JL, Laing GL, Clarke DL Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: a South African experience. *Emerg Med Australas*. 2018. DOI: 10.1111/1742-6723.12985.

Emergency Medicine Australasia

*Emergency Medicine Australasia* (2018) doi: 10.1111/1742-6723.12985

ORIGINAL RESEARCH

# Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: A South African experience

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## Abstract

***Objective***: Routine immobilisation of the cervical spine in trauma has been a long established practice. Very little is known in regard to its appropriateness in the specific setting of isolated traumatic brain injury secondary to gunshot wounds (GSWs).

***Methods***: A retrospective study was conducted over a 5 year period (January 2010 to December 2014) at the Pietermaritzburg Metropolitan Trauma Service, Pietermaritzburg, South Africa in order to determine the actual incidence of concomitant cervical spine injury (CSI) in the setting of isolated cerebral GSWs.

***Results***: During the 5 year study period, 102 patients were included. Ninety-two per cent (94/102) were male and the mean age was 29 years. Ninety-eight per cent of the injuries were secondary to low velocity GSWs. Twenty-seven (26%) patients had cervical collar placed by the Emergency Medical Service. The remaining 75 patients had their cervical collar placed in the resuscitation room. Fifty-five (54%) patients had a Glasgow Coma Scale (GCS) of 15 and underwent plain radiography, all of which were normal. Clearance of cervical spine based on normal radiography combined with clinical assessment was achieved in all 55 (100%) patients. The remaining 47 patients whose GCS was <15 all underwent a computed tomography (CT) scan of their cervical spine and brain. All 47 CT scans of the cervical spine were normal and there was no detectable bone or soft tissue injury noted.

***Conclusion***: Patients who sustain an isolated low velocity cerebral GSW are highly unlikely to have concomitant CSI. Routine cervical spine immobilisation is unnecessary, and efforts should be directed at management strategies aiming to prevent secondary brain injury. Further studies are required to address the issue in the setting of high velocity GSWs.

**Key words:** *cerebral gunshot wounds, cervical spine immobilisation, traumatic brain injury.*

## Key findings

- Civilian cerebral GSWs are predominantly related to low velocity firearms.
- Concomitant cervical spine injury associated with isolated cerebral GSWs are rare.
- Routine cervical spine immobilisation is unnecessary.

## Introduction

The risk of concomitant cervical spine injury (CSI) associated with traumatic brain injury (TBI) has been reported to range from 1.7% to 15%.[1–5] Most of the literature on CSI in association with TBI is based on the experience with blunt trauma.[1–5] The fear of a missed CSI, along with the potential medicolegal consequences has led to the widespread precautionary use of routine cervical spine immobilisation until 'cervical spine clearance' is achieved.[1,6] This practice has been widely embraced and extended to include all patients with TBI regardless of mechanism. Patients with an isolated low velocity cerebral GSW generally undergo spinal immobilisation with a cervical collar.[7,8] This established practice has recently been called into question.[1] In the context of TBI, a rigid cervical collar impairs jugular venous return and can potentially exacerbate raised intra-cranial pressure (ICP).[9] In addition, it can create difficulties with endotracheal intubation, which further increases the risk of hypoxia. Both hypoxia and increased ICP are detrimental to the already injured brain.[10] There is a general paucity of literature on the topic and the aim of this study was to review our own experience of managing patients with an isolated cerebral GSWs in order to determine the incidence of concomitant CSI.[8]

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*Accepted 4 March 2018*

## Materials and methods

### *Clinical setting*

This was a retrospective study undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Our electronic regional trauma registry was reviewed over a 5 year period from January 2010 to December 2014. Ethics approval for this study and for maintenance of the registry was formally endorsed by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (KZN) (reference: BE 207/09 and BCA 221/13). The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of KZN province. It is one of the largest academic trauma centre in the province and serves as the tertiary referral centre for 19 other hospitals within the province, with a total catchment population of over 3 million. Approximately 4000 trauma cases are admitted to the PMTS each year, with over 50% being due to penetrating trauma. This is a direct reflection of the high incidence of firearm related interpersonal violence and criminal activities throughout the entire province.

### *The study*

All patients who sustained an isolated cerebral GSW were included in the study. An isolated cerebral GSW was defined as bullet penetration limited to the cranium itself. Those with additional and/concurrent injury to the face or neck were excluded, as well as those with concurrent GSWs to other body regions (e.g. chest, abdomen). Basic demographic data were reviewed. Further data review included the mode of injury (assault, suicide or accident), types of firearms, vital signs (physiological parameters on arrival), physical examination findings, admission Glasgow Coma Scale (GCS), reports from radiological investigations and the clinical outcome on discharge (or death).

### *Management protocol*

The initial management of all patients with cerebral GSWs closely follows the *Advanced Trauma Life Support (ATLS©)* principles. A rigid cervical collar is applied on arrival in the resuscitation room, as for any patient with TBI. In those who arrived at our trauma centre with a cervical collar already placed by the Emergency Medical Service (EMS) personnel, the collars were not removed until our cervical spine clearance protocol had been completed (Fig. 1). The decision to place a cervical spine collar in the prehospital setting is at the discretion of the transporting EMS personnel. There is currently no prehospital protocol for cervical spine immobilisation specifically pertaining to cerebral GSWs.

Our current trauma centre protocol for cervical spine clearance (Fig. 1) in the context of cerebral GSWs is as follows: Patients with a GCS of 15 and intact sensorium underwent a standard cervical spine plain radiograph series (anterior–posterior, lateral and open mouth views). Clearance is achieved using a combination of both radiological and clinical assessment. Patients with GCS <15, or if there is concern regarding the reliability of clinical examination findings, were imaged with computed tomography (CT) scan, which is performed in the same setting as the CT brain scan. Unless the patient is dead on arrival, every patient who sustained a cerebral GSW undergoes a CT brain regardless of the GCS. CSI was described as the presence of any injury on cervical spine CT. All CT scans performed at our institution were reviewed by both the consultant trauma surgeon and the duty consultant radiologist. The images and the final reports of all radiological investigations were formally reviewed as a part of this study.

### *Definitions*

The US army defines a high velocity hand gun as having a muzzle velocity of between 3500 and 5000 ft per second.[1] Hand guns with a muzzle velocity lower than this are defined as low velocity hand guns. These definitions are used at our institution.

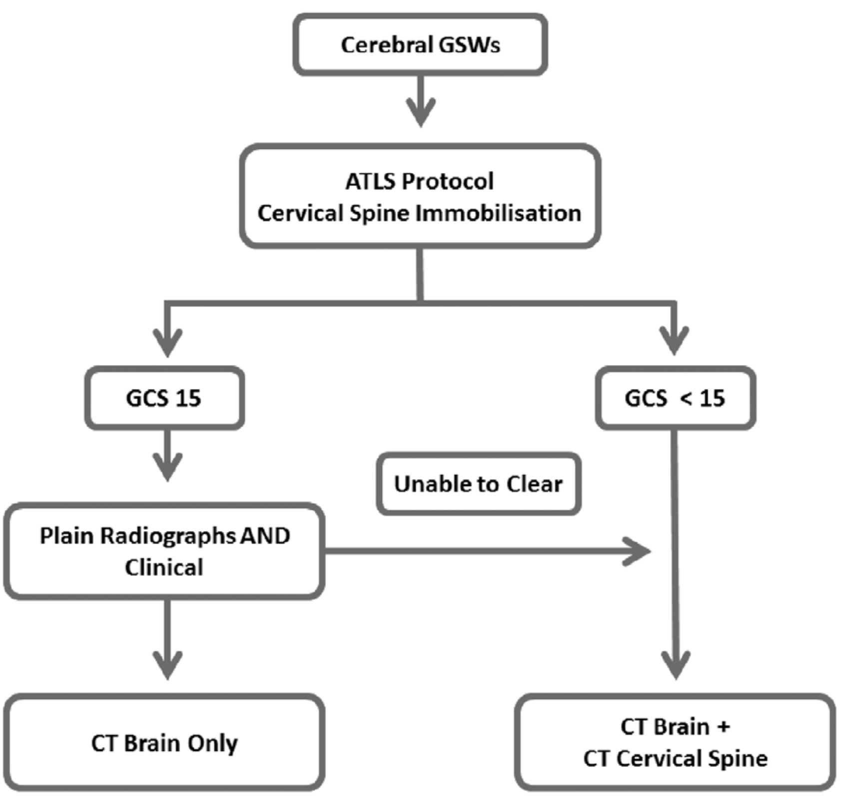


**Figure 1.** *Cervical spine clearance protocol for cerebral GSWs.*

## Results

### Demographics and injury pattern

During the 5 year study period, a total of 102 patients with isolated cerebral GSWs were included. Ninety-two per cent (94/102) were male and the mean age was 29 years (standard deviation [SD]: 8 years). Ninety-four per cent (94/102) of injuries were related to interpersonal violence (assaults). The remaining 6% (6/102) were attempted suicides, all of whom were male. Ninety-eight per cent (100/102) of all cerebral GSWs involved the use of low velocity firearms (LVF), and the remaining 2% (2/102) were high velocity firearms (HVF). This preponderance for low velocity weapons is reflective of the weapons available to the urban youth in South Africa.

### Clinical presentations

The mean (SD) values of physiological parameters on arrival were as follows: heart rate: 85/min (24), systolic blood pressure: 124 mmHg (22), temperature: 36 (1). The mean (SD) GCS on arrival was 12 (5). Thirty per cent (31/102) of all patients had visible brain matter (VBM) oozing from the wound. All 102 patients underwent CT scan of the brain.

### Cervical spine clearance

Twenty-seven (26%) patients had cervical collar placed by the EMS personals prior to arrival at our trauma centre. The remaining 75 patients had their cervical collar placed in the trauma resuscitation room on arrival. Fifty-five (54%) patients had a GCS of 15 and underwent plain radiography of the cervical spine. All of these were found to be technically adequate and repeated/additional views were deemed not to be necessary. Clearance of cervical spine based on normal radiography combined with clinical assessment was achieved in all 55 (100%) patients. The remaining 47 patients whose GCS was <15 all underwent a CT scan of the cervical spine on the same occasion as the CT brain. All 47 CT cervical spine were normal and there no detectable bone or soft tissue injury noted on any of the reports.

### Final clinical outcome

Of the 102 patients, 22% (22/102) died during the admission. The remaining 80 patients (78%) survived to discharge to rehabilitation. There were no CSI in any of the patients.

## Discussion

The reported incidence of CSI associated with TBI is up to 15%.[2–6] However, this represents all TBI, including those from both blunt and penetrating mechanisms.[2–6] TBI from blunt trauma has been studied extensively. The practice of precautionary cervical spine immobilisation with a rigid collar has been extended to all patients with TBI regardless of the mechanism.[8–10] Rigid cervical spine immobilisation is potentially hazardous for several reasons. The application of a rigid cervical collar impairs jugular venous return, which may lead to an increase in ICP.[10] In addition, early endotracheal intubation to secure the airway, and adequate oxygenation to maintain cerebral metabolism are all critical in preventing secondary brain injury.[11] Rigid cervical collar renders intubation much more difficult and this may expose patients to longer period of hypoxia and hypercarbia.[9,11] A recent review by Sundstrom *et al.* concluded that the current existing evidence for the use of cervical collars is weak.[2] The current practice is primarily historical and is not underwritten by robust evidence.[2] Furthermore, it appears that the potentially harmful effects from rigid cervical collar are often under appreciated.[2]

Currently, there is very limited literature on the actual incidence of CSI in the context of isolated cerebral GSWs.[8] There are only four studies published to date over the past two decades.[8,9,11,12] Kennedy *et al.* from Los Angeles reported the first series of 105 patients with isolated GSWs limited to the cranium, none of which had concomitant CSI.[9] Findings from subsequent studies by Chong *et al.* in Houston[12] and Kaups *et al.* in Fresno[11] were both consistent with that of Kennedy *et al.* Furthermore, Kaups *et al.* also noted that more intubation attempts were required in patients with rigid cervical spine immobilisation.[11] In another study of 174 patients by Lanoix *et al.* from New York, none of those who underwent radiological investigations had a CSI. It was further concluded that cervical collar, as well as radiological clearance of cervical spine were unnecessary.[8] Table 1 summarises the literature to date.

Our present study is consistent with the literature, in that none of our 102 patients had any detectable concomitant CSI. This has important implications for our resuscitation strategies in these patients.[13] In addition to the potentially harmful effect resulted from indiscriminate use of rigid cervical collar, superfluous radiological investigations are costly and further burden an already overstretched healthcare system.[13,14] CSI

**TABLE 1.** *Incidence of concomitant cervical spine injury (CSI) in patients with isolated cerebral gunshot wounds (GSWs) (1998–2016)*

| Author(s) | Country | Year | Isolated GSWs | CSI incidence |
|---|---|---|---|---|
| Current study | South Africa | 2016 | 102 | 0 |
| Lanoix *et al.*[7] | USA | 1999 | 174 | 0 |
| Kaups *et al.*[10] | USA | 1998 | 202 | 0 |
| Chong *et al.*[18] | USA | 1998 | 53 | 0 |
| Kennedy *et al.*[8] | USA | 1994 | 105 | 0 |

in isolated low velocity cerebral GSWs has not previously been subjected to any formal review in South Africa.[15,16] Management approaches continue to vary. Our current study suggests that concomitant CSI in the context of isolated low velocity cerebral GSWs almost never occurs. In our experience, the routine application of a cervical spine collar to patients with a low velocity isolated cerebral GSW is unnecessary, potentially harmful and should be avoided.

GSWs from high velocity firearms are different to those of low velocity, as they are associated with greater energy transfers (kinetic energy = ½ m $v^2$) and thus greater tissue destruction. Following a low velocity GSW, the neurological injury is confined to tissue destruction along the missile tract. However, a high velocity GSW produces cavitation and shock waves, causing more severe brain damage and bone fragmentation.[17] More research is needed to establish if rigid cervical supine immobilisation is necessary following a high velocity cerebral GSW.

## Conclusions

Patients who sustain an isolated low velocity cerebral GSW are highly unlikely to have a concomitant CSI. Routine cervical spine immobilisation is unnecessary and potentially harmful. Efforts should instead be directed at management strategies aiming to prevent secondary brain injury in order to optimise outcome for these patients. More research is required to establish if the same practice can be followed following a high velocity cerebral GSW.

### *What this research adds*

Very little is known in regard to the appropriateness of routine cervical spine immobilisation in the specific setting of isolated cerebral GSWs, with only four studies published over the past two decades on this topic. These studies suggest isolated low velocity cerebral GSW rarely have concomitant CSI. Despite this, cervical immobilisation continues to be routinely used across the world. Our current study concurs with the literature, suggesting routine cervical immobilisation is not evidence based and is unnecessary.

### *Competing interests*

VYK, JLB, GLL and DLC are all current ATLS instructors.

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# Conclusions

Cerebral GSWs in our setting in South Africa occur primarily in young males who are predominantly victims of interpersonal violence involving low-velocity firearms, with self-harm and accidental GSWs being uncommon. The overall mortality is high. Rural patients have a disproportionately higher mortality rate than their urban counterparts. This is almost certainly related to prolonged transfer times from rural locations to our urban trauma centre. For those who do survive the transfer to our trauma centre, the Baragwanath mortality-prediction score accurately predicted non-survivors and was directly applicable to our patient cohort. The Maritzburg score is a simplified mortality-prediction score and consists of two parameters (the presence of visible brain matter and a GCS motor score < 5) that allows simpler and more accurate identification of non-survivors. In addition, an elevated serum lactate level on arrival at hospital is closely correlated to adverse outcome and is an independent predictor of in-hospital mortality. Patients with isolated cerebral GSWs are highly unlikely to sustain concomitant cervical spine injury and routine cervical spine immobilisation is unnecessary. Efforts should instead be directed at management strategies aiming to prevent secondary brain injury in order to optimise patient outcome.

# Appendices

# Appendix A:

## MD Research Project Proposal

*Approved by the Faculty of Health Sciences Ad Hoc Research Committee on 07/05/2018*

**Project Title:**

The spectrum and clinical outcome of civilian cerebral gunshot wounds at a major trauma centre in South Africa.

**Background:**

Cerebral gunshot wounds (GSWs) are among the most lethal of traumatic brain injuries [1-6]. Over 90% of victims die before reaching hospital, and a further 50% die in the resuscitation room [5]. Civilian cerebral GSWs are relatively uncommon outside of South Africa and the United States [1]. Firearm-related trauma is exceedingly common in South Africa, and the current situation has been termed a ‘malignant epidemic’ [7]. In a 2009 forensic study by the South African Medical Research Council (SAMRC), it was estimated that 98% of all firearms deaths are caused intentionally, and 88% of these are homicides [8,9].

Several high-profile GSW cases have attracted international media attention, especially the case of US congresswoman Senator Gabrielle Gifford who was injured in Arizona [10]. However, this attention is in stark contrast to South Africa, where trauma is a largely neglected condition [7]. The vast majority of victims with cerebral GSWs in South Africa are managed by trauma surgeons and general surgeons, and only a small sub-set is exposed to direct involvement by a neurosurgical specialist [11]. This is a reflection of the shortage of resources that are perennially insufficient to manage the massive burden of trauma across

South Africa. Furthermore, the geographical barriers experienced by rural patients in accessing appropriate trauma care remain a major problem [12].

Most evidence for the management of cerebral GSWs is based on historical experience from the Vietnam War [2-6]. There are only two published studies originating from South Africa that describe the spectrum of injuries for GSWs, and both seminal papers were from the University of the Witwatersrand in Johannesburg [1,13]. The mortality rates reported by Stoffel, *et al.* from Baragwanath Hospital and Glapa, *et al.* from Milpark Hospital were 27% and 58% respectively [1,13]. A clinical scoring system was also proposed by Stoffel, *et al*. that is useful for predicting mortality, but has never been validated on any other patient population, either locally or abroad [1].

**Rationale for Proposed Project:**

Due to the paucity of literature in this important area, a research project was initially proposed based on cumulative clinical experience from Pietermaritzburg Metropolitan Trauma Service (PMTS) in Pietermaritzburg, KwaZulu-Natal (KZN). The primary focus of this project is to address the deficiency in current knowledge relating to cerebral GSW injuries within the specific context of South Africa. Despite resource constraints in South Africa, it has a proud history of providing major contributions to many areas of trauma care internationally. This project was inspired by the pioneering work at University of the Witwatersrand.

**The Proposed Project:**

This MD research project is based on a series of six published papers (i.e. retrospective publications as per the University requirement). The candidate is the first author for all six papers, which have been published in international, peer-reviewed journals. These papers have been published under the Department of Surgery, University of the Witswaterand as well as the Pietermaritzburg Metropolitan Trauma Service. A summary of these publications is to be integrated into a final MD thesis to be presented for examination as soon as admission is approved by the Faculty.

**Objectives:**

The objectives of this MD research project are divided into six themes that are interrelated. Each theme forms an individual chapter within the MD thesis. All six papers have been published (or accepted for publication but in press).

**Objective 1:**

To describe the spectrum and clinical outcome for patients who have sustained cerebral GSWs in the civilian population.

***Publication:***

**Kong VY, Odendaal JJ, Sartorius B, Clarke DL, Brysiewicz P, Jerome E Bruce JL, Laing GL. Civilian cerebral gunshot wounds: a South African experience. *ANZ J Surg*. 2017: 87(3):186-9.**

***Journal:*** Australian and New Zealand Journal of Surgery.

**Objective 2:**

To describe the discrepancy of clinical outcomes between rural and urban patients who have sustained cerebral GSWs.

***Publication:***

**Kong VY, Clarke DL, Laing GL, Bruce JL, Brysiewicz P, Sartorius B, Odendaal JJ. Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality than in urban patients. *Eur J Trauma Emerg Surg*. 2017.**

***Journal:*** European Journal of Trauma and Emergency Surgery

**Objective 3:**

To validate the Baragwanath mortality-prediction score for a similar patient population in western KwaZulu-Natal.

***Publication:***

**Kong VY, Oosthuizen GV, Weale R, Sartorius B, Bruce JL, Clarke DL. Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: The Pietermaritzburg experience. *Eur J Trauma Emerg Surg*. 2018; 44(4):615-620.**

***Journal:*** European Journal of Trauma and Emergency Surgery

**Objective 4:**

To propose an alternative simplified mortality prediction score based on clinical parameters that are immediately available in the resuscitation room.

***Publication:***

**Kong VY, Clarke DL, Oosthuizen GV, Esterhuizen T, Bruce JL, Laing GL, Odendaal JJ. Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: The Maritzburg Score. *Ann R Coll Surg Engl*. 2018; 100(2):97-100.**

***Journal:*** Annals of The Royal College of Surgeons of England

**Objective 5:**

To review the value of serum-lactate levels as a predictor of in-hospital mortality.

***Publication:***

**Kong VY, Weale R, Sartorius B, Oosthuizen GV, Bruce JL, Laing GL, Clarke DL. A raised serum lactate level is an independent predictor of in-hospital mortality in-patients with isolated cerebral gunshot wounds. *S Afr Med J*. 2018; 108(5):413-417.**

***Journal:*** South African Medical Journal

**Objective 6:**

To review the role of cervical spine immobilisation with rigid collar in the initial management of patients with cerebral GSWs.

***Publication:***

**Kong VY, Weale R, Sartorius B, Bruce JL, Laing GL, Clarke DL Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: a South African experience. *Emerg Med Australas*. 2018.**

***Journal:*** Emergency Medicine Australasia

**Materials and Methods:**

***The Clinical Setting:***

The proposed study was a retrospective project undertaken at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. Electronic regional trauma registry data were available for review covering a five-year period, from January 2010 to December 2014. KwaZulu-Natal is located on the eastern coast of South Africa, and has a population of over 11 million. Fifty per cent of the population live in rural areas. The PMTS provides definitive trauma care to the city of Pietermaritzburg, which is the capital of KwaZulu-Natal (KZN) province, and PMTS serves as the trauma referral centre for 19 other rural hospitals within the province, with a total catchment population of over three million.

The catchment area is divided into two health districts: the urban district (UD), which includes the city of Pietermaritzburg and the surrounding suburban areas, and the rural district (RD), which includes all areas outside of UD geographical boundaries, with local rural hospitals providing basic, non-specialist healthcare. Approximately 4,000 trauma cases are admitted to the PMTS per annum, with over 50% due to penetrating trauma. This is a direct reflection of the high incidence of firearm-related inter-personal violence and serious crime that is experienced throughout the province.

***Study Type:***

The proposed research was a retrospective study based on a review of an anonymised dataset from our regional trauma registry. The study did not involve any direct patient contact and there were no interventions. This was a self-funded research project and no external funding was required. The research student had full access to the regional trauma registry and the research facilities available at the PMTS.

***Ethics Approval:***

Ethics approval for this study and for a review of the registry was formally endorsed by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (reference: BCA 221/13).). This is fully compliant with local IRB requirement and the primary researcher holds a current ICH Good Clinical Practice Certificate (06/03/2018): 003026708.

***Research Methodology:***

***Objective 1:***

All patients who sustained a single, isolated cerebral GSW were included in the study. Those with concurrent GSWs to other body regions were excluded. All patients who died in transit or who were pronounced dead on arrival (and so taken directly to the mortuary), were considered further. Basic demographic data were reviewed, and, where available, specific information were sought regarding the geographical location of incidents within the catchment area, as well as the documented approximate time of injury (if known). A further data review included the mode of injury (assault, suicide or accident), the type of firearm used, vital signs (i.e. physiological parameters on arrival), any physical examination findings, the Glasgow Coma Scale (GCS) score, and the final clinical outcome. The conventional classifications of injury severity based on GCS were used to group all patients into three categories: Mild (13–15), Moderate (9–12) and Severe (3–8). The data were processed and analysed using Stata 13.0 (StataCorp LP, College Station, TX, USA). Continuous variables were summarised using mean and standard deviations (SD). The median and inter-quartile range were presented instead when there was evidence of skewing/asymmetry relating to a continuous variable. Differences in means between continuous variables, such as age by urban/rural setting, were assessed using the Student’s T-test. Furthermore, associations between categorical variables and the urban/rural setting were assessed using the Pearson chi-squared ($\chi 2$) test or Fisher's exact test. The significance cut-off was 5%.

***Objective 2:***

Specific information was sought regarding the geographical location of incidents within the catchment area, as well as the time of injury, and the ambulance transport time from the location of the incident to our trauma centre. Patients who sustained injuries within the UD were classified as ‘urban’, while those who sustained injuries within the RD were classified as ‘rural’ patients. Further data review included the mode of injury (namely, assault, suicide or accident), the type of firearm used, vital signs on arrival, physical examination findings, the Glasgow Coma Scale (GCS) score, and the final clinical outcome. The conventional classification of injury severity as based on GCS were used to group all patients into three categories: Mild [13–15], Moderate [9–12] and Severe [3–8]. The data were processed and analysed using Stata 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). The continuous variables were summarised using mean and standard deviations (SD). Differences in means between continuous variables, such as age by urban/rural setting, were assessed using the student's T-test. Any associations between categorical variables and an urban/rural setting were assessed using the Pearson Chi squared ($\chi 2$) test, or Fisher's exact test. The significance cut-off was 5%.

***Objective 3:***

All patients with cerebral GSW were categorised using the Baragwanath ABC score, and outcomes were compared directly with published data from Stoffel, *et al.* The data were processed and analysed using Stata 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) and the statistical package R 3.2.4 (R Core Team, 2016 R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org). Continuous variables were summarised using mean and standard deviations (SD). Associations between categorical variables and survival were assessed using the Pearson chi-squared ($\chi 2$) test or Fisher's exact test. A 'p' value of less than 0.05 was deemed statistically significant. Several criteria were applied to identify optimal cut-offs, using receiver operating characteristic (ROC) curves. An optimal breakpoint of a 2 + ABC score for mortality prediction based on PMTS data was identified using a positive predictive value (PPV) optimisation procedure. The diagnostic capability (sensitivity, specificity, PPV, and NPV) of this threshold score was estimated along 95% confidence intervals.

***Objective 4:***

Data review included the mode of injury (assault, suicide or accident), the type of firearm used, vital signs (physiological parameters on arrival), any physical examination findings, the

GCS, and the final clinical outcome. The GCS was further divided into its component scores of: eye opening, vocal response and motor response, for each patient. The IBM SPSS version 23 statistical program was used to analyse the data. Crude associations between independent variables and the outcome of death or survival were assessed using the Pearson chi-squared ($\chi 2$) test or Fisher's exact test, as appropriate, in the case of categorical variables. Continuous variables were tested using T-tests or Mann- Whitney non-parametric tests, as appropriate. A receiver-operating characteristic analysis was undertaken to determine the optimum cut-off points for each variable, in order to predict mortality. Multiple logistic regressions were used to determine predictors that are independently and significantly associated with mortality, and to determine a simple clinical model used to predict mortality with a high level of accuracy. A backward stepwise model was used, with entry and exit probabilities set at 0.05 and 0.1, respectively.

***Objective 5:***

The serum-lactate levels were arbitrarily divided into four categories: A: 0-1.99 mmol/L, B: 2-3.99 mmol/L, C: 4-5.99 mmol/L, D: ≥6 mmol/L. The mean serum-lactate levels between survivors and non-survivors were compared using the student's T-test. Associations between mortality and serum-lactate categories, as well as other categorical explanatory variables, were assessed using the Pearson chi-square ($\chi 2$) test or Fisher's exact test, if an expected cell count has fewer than five observations. The multi-variable adjusted association between lactate and in-hospital mortality was also assessed using a logistic regression, to account for the potential confounding influence of other risk factors.

***Objective 6:***

Data review included the mode of injury (assault, suicide or accident), the type of firearm used, vital signs (physiological parameters on arrival), any physical examination findings, admission Glasgow Coma Scale (GCS) score, reports from radiological investigations, and the clinical outcome on discharge (or death). The focus here was on the cervical spine immobilisation protocol that is in widespread use among pre-hospital and trauma centres across the country, regardless of mechanism. This was done to specially address the role of the cervical spine collar in cerebral GSWs.

***Supervisor:***

**Professor Damian Clarke**, MBBCh(Wits), MMedSci, MPhil, MBA, PhD, FCS(SA)

Associate Professor of Surgery, University of the Witwatersrand, Johannesburg

Professor of Surgery, University of KwaZulu Natal, Durban

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# Appendix B: Ethics Approval

**UNIVERSITY OF KWAZULU-NATAL**
**INYUVESI YAKWAZULU-NATALI**

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Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

23 July 2018

Dr G Laing
Town Bush Road
Chase Valley
Pietermaritzburg
grantlaing@me.com

**PROTOCOL: Class approval for a database. REF: BCA221/13**

**RECERTIFICATION APPLICATION APPROVAL NOTICE**

Approved: **07 August 2018**
Expiration of Ethical Approval: **06 August 2019**

I wish to advise you that your application for Recertification received on 29 June 2018 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

This committee will be notified of the above approval at its next meeting taking place on **14 August 2018.**

Yours sincerely

**Prof V Rambiritch**
Chair: Biomedical Research Ethics Committee

# Appendix C: Turnitin Report

As per the requirement of the Faculty of Health Science, this MD thesis was submitted to *Turnitin*, a plagiarism-detection service, for assessment. This was performed on my behalf by Ms Denise Nicholson, Scholarly Communications Librarian at the Wartenweiler Library of the University of the Witwatersrand (Contact: Email:denise.nicholson@wits.ac.za. Tel: +27(0)117171929). The *Turnitin* report is below.

Please note that the seemingly high percentages of similarity are a direct consequence of the following. The MD thesis at the University of the Witwatersrand is a compilation of a series of published papers within a specific theme that forms a coherent piece of scientific work in a form of a thesis for examination. All of the papers were authored by myself. As the papers included had already been published and were available in the public domain, it is inevitable that these would all have been detected by *Turnitin* when their database was interrogated. Secondly some of the similarities, especially the factual description of our trauma centre, sentence structures, and general writing style that were detected were almost always related to my other publications not included in this thesis. To date, I have authored (or co-authored) over 100 papers published in peer-reviewed national and international journals. I have collaborations with numerous international centres which have culminated in many joint publications. The vast majority of these are in the trauma surgery domain. This is a limitation of the *Turnitin* reporting system. I believe that all the text, where applicable, is appropriately referenced and I am certain that this in no way remotely represents any form of plagiarism. I am confident that this will be taken into consideration during the examination process.

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*by* Denise Nicholson

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ORIGINALITY REPORT

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| 1 | Victor Kong, Jocinta Odendaal, Benn Sartorius, Damian Clarke, Petra Brysiewicz, Ellen Jerome, John Bruce, Grant Laing. "Civilian cerebral gunshot wounds: a South African experience", ANZ Journal of Surgery, 2017<br>Publication | 9% |
| 2 | V. Y. Kong, G. V. Oosthuizen, B. Sartorious, J. L. Bruce, G. L. Laing, R. Weale, D. L. Clarke. "Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: the Pietermaritzburg experience", European Journal of Trauma and Emergency Surgery, 2017<br>Publication | 3% |
| 3 | V. Y. Kong, J. L. Bruce, B. Sartorius, G. L. Laing, J. Odendaal, P. Brysiewicz, D. L. Clarke. "Civilian cerebral gunshot wounds in rural South African patients are associated with significantly higher mortality rates than in urban patients", European Journal of Trauma and Emergency Surgery, 2017 | 3% |

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unnecessary in patients with isolated cerebral gunshot wounds: A South African experience", Emergency Medicine Australasia, 2018
Publication

| | | |
|---|---|---|
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