

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.

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 = $\frac{1}{2}mv^2$) 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 (χ^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 (χ^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 (χ^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 (χ^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 (χ^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:

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Appendix B: Ethics Approval



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23 July 2018

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

RECERTIFICATION APPLICATION APPROVAL NOTICE

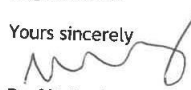
Approved: 07 August 2018
Expiration of Ethical Approval: 06 August 2019

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

Publication

13

J J P Buitendag, A Ras, V Y Kong, J L Bruce, G L Laing, D L Clarke, P Brysiewicz. "Validation of the Simplified Motor Score in patients with traumatic brain injury at a major trauma centre in South Africa", *South African Medical Journal*, 2018

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17

G.V. Oosthuizen, R. Weale, V.Y. Kong, J.L. Bruce, R.J. Urry, G.L. Laing, D.L. Clarke. "The effect of a concomitant renal injury on the outcome of colonic trauma", *The American Journal of Surgery*, 2017

Publication

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