Study Protocol

Ability of Infrascanner 2000 to predict post-traumatic cranial hemorrhage volume in low-resource settings: a protocol for a multi-center prospective, observational study

Laura L. Fernandez, Dylan P. Griswold, Sarita Aristizabal, Diana M. Sanchez and Andres M. Rubiano

Abstract

Low- and middle-income countries experience three times more traumatic brain injury (TBI) cases when compared with their high-income country counterparts. The quality of care patients receive in the prehospital setting and emergency department settings are highly variable and often dependent on computed tomography (CT) availability. The implementation of a handheld device that is able to reliably diagnose intracranial hemorrhage (ICrH) in TBI patients is needed in these settings where CT is unavailable. The Infrascanner has shown promise to detect intracranial bleeds in patients with moderate TBI. We aim to determine the correlation between the coefficient provided by the Infrascanner compared to the post-traumatic supratentorial hemorrhagic collections volume in patients with surgical indication in different trauma centers. This is a multi-center prospective observational study that will be carried out in three trauma centers in Colombia, Guatemala and Pakistan. We calculated a sample size of eighty-six patients with mild, moderate or severe TBI ≥ 15 years old who have a supratentorial hemorrhage abnormality that requires neurosurgical intervention. The Infrascanner’s ability to detect IChR in patients with surgical indications associated to hemorrhage volume when compared with CT is the primary outcome measure. Secondary outcome measure is the correlation of the mean of the six Infrascanner measurement values compared with volume of ICrH as measured from the six manual head CT segmentation measurements. ICrH volume correlation and agreement will be evaluated by the Pearson coefficient and Bland-Altman analysis, and a linear regression analysis will be performed in order to predict IChR from the Infrascanner measurement.

INTRODUCTION

Globally, the incidence of traumatic brain injury (TBI) is 369 per 100 000 according to 2016 data [1]. By comparison, the incidence of cancer is 198 per 100 000 [2]. Low- and middle-income countries (LMICs) experience nearly three times more cases of TBI when compared with high-income countries (HICs) [3]. This amounts to 80% of all TBI cases occurring in LMICs. The annual cost of TBI care is >400 billion USD [4]. However, the greatest threat to LMICs is the indirect cost of TBI. This includes loss of productivity, disability, reduced quality of life and the need for family to take care of the patient, which has its own indirect costs in loss of productivity [5]. These indirect costs are rarely accounted for. Isolated or associated epidural, subdural and intraparenchymal hematomas are common entities during a TBI event, and early diagnosis and treatment minimize secondary injuries to the patient [6]. The gold standard for diagnosis of intracranial hemorrhages (ICrHs) due to TBI is computed tomography (CT). There is less than one CT scanner per million in LMICs compared to 40 per million in HICs [7]. The lack of trained health personnel and inadequate maintenance are also a barrier [8]. The fast identification of intracranial lesions and the therapeutic window in TBI patients is critical. Treatment delay is associated with neurological deterioration, higher 24-h mortality and 30-day mortality rates. A cohort of 6278 in a LMIC demonstrated that 34% of TBI patients received adequate treatment within 10–60 min after admission and that 22% received adequate treatment within ≥61 min [9]. Thus, the need for research on the detection of lesions and
decision-making for the neurocritical patient to save time has increased.

The Infrascanner 2000™ is a handheld and easy-to-use device that uses a near-infrared spectroscopy system to detect intracranial hematomas based on the near-infrared light hemoglobin absorption. Previous studies have reported that the Infrascanner has a sensitivity of 75–100% and a specificity of 81–97% for detecting intracranial hematomas. However, no studies on the relationship of the coefficient given by the Infrascanner and the volume of the hemorrhage have been published. Therefore, we aim to determine the correlation between the coefficient provided by the Infrascanner compared to the post-traumatic supratentorial hemorrhagic collections volume in patients with surgical indication in different trauma centers.

MATERIALS AND METHODS
Study design, setting and duration
This is a multi-center prospective observational study. The study will be conducted at Valle Salud clinic in Cali, Colombia, as well as two other trauma referral centers in Guatemala and Pakistan. The study will be conducted from February 2022 until data from the 86 patients have been collected. We expect the study to conclude by January 2023.

Eligibility criteria for patients
The study will include TBI patients who meet the following criteria:
- Patients ≥15 years old.
- Brain injury of mild, moderate and severe TBI according to GCS.
- Patients with supratentorial hemorrhage abnormality (subdural, epidural, intraparenchymal and contusion) who require surgical intervention according to CT scan findings.

The study will exclude TBI patients who meet the following criteria:
- Pediatric patients (<15 years old).
- Patients with subarachnoid hemorrhage.
- Patients with hemorrhagic abnormalities not requiring surgical intervention.

Data collection
Data collection will be performed in a trauma center in each of the three participating countries comprising of Colombia, Guatemala and Pakistan. Patients presenting to the ED with indications of TBI will undergo a head CT scan. If a hemorrhagic lesion requiring neurosurgical intervention is identified, LF and DG will each take three serial measurements with the Infrascanner 2000™ device (InfraScan, Inc, Philadelphia, PA, USA) according to the device protocol (REF).

Data entry
Data of this study will be captured by the REDCap system hosted by the MEDITECH Foundation.

Primary outcome measures
The primary outcome measure is the Infrascanner’s ability to detect IChR in patients with surgical indications associated to hemorrhage volume when compared with the CT as determined by current surgical guidelines recommendations.

Secondary outcome measures
The secondary outcome measure is the correlation of the mean (delta) of the six Infrascanner measurement values compared with volume of ICrH as measured from the six manual head CT segmentation measurements for inter- and intra-rater reliability analyses.

Data source
Each patient will be assigned a unique registration number within the study to ensure confidentiality and proper treatment of the data.

Statistical analysis plan
The Infrascanner measurement values will be evaluated compared to manual segmentations for their volumetric accuracy and reliability. ICrH volume correlation and agreement will be evaluated by the Pearson coefficient and Bland-Altman analysis, respectively. The intraclass correlation coefficient will be used to measure the inter-rated reliability and repeatability between the users. The standard error of measurement and 95% minimal detectable change will be calculated to examine the absolute reliability.

A linear regression analysis will be performed in order to predict IChR from the Infrascanner measurement. All statistical analyses will be performed using SPSS.

ETHICS AND DISSEMINATION
Ethical approval
This study will be conducted according to the principals of the declaration of Helsinki. Ethical approval
was granted by the Ethics Committee of MEDITECH Foundation and the Valle Salud Clinics Network in Cali, Colombia. Each patient will be asked to sign the informed consent before participation in the study.

**Interference with patient management**
This is an observational, prospective, observational study and thus will not interfere with, alter or substitute patient management.

**Risks and benefits**
This study does not interfere with patient management and thus will not interfere with patient management. Patients are not exposed to any direct risks when participating in this study.

While direct benefits are not provided to the patients, the results will benefit them indirectly by identifying stronger correlates of volume of ICrH. This will better predict the patient’s need for surgical intervention.

**Publication and dissemination plan**
We plan to publish this study in an international peer-reviewed journal.

**CONCLUSION**
This is a novel study that has yet to be performed with the Infrascanner. It will elucidate the extent to which Infrascanner can be used to detect hemorrhage volume and, subsequently, the patient’s need for surgical intervention.

**CONFLICT OF INTEREST STATEMENT**
None declared.

**FUNDING**
MEDITECH Foundation internally funds the REDCap system used for this study. Mr Griswold is funded by the Gates Cambridge Trust (OPP1144).

**REFERENCES**
1. James SL, Theadom A, Ellenbogen RG, Bannick MS, Montjoy-Venning W, Lucchesi L, et al. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019;18:56–87.
2. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 2019;144:1941–53.
3. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung Y-C, Punchak M, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg 2019;130:1080–97.
4. Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic brain injury-related emergency department visits, hospitalizations, and deaths - United States, 2007 and 2013. Morbidity Mortal Wkly Rep Surveillance Summ Wash D C 2002 2017;66:1–16.
5. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol 2017;16:987–1048.
6. Aromatario M, Torsello A, D’Errico S, Bertozzi G, Sessa F, Cipolloni L, et al. Traumatic epidural and subdural hematoma: epidemiology, outcome, and dating. Medicina 2021;57:125.
7. Frija G, Blažič I, Frush DP, Hierath M, Kawooya M, Donoso-Bach L, et al. How to improve access to medical imaging in low- and middle-income countries? Eclinicalmedicine 2021;38:101034.
8. Vasan A, Friend J. Medical devices for low- and middle-income countries: a review and directions for development. J Medical Devices 2020;14:010803.
9. Gupta S, Khajanchi M, Kumar V, Raykar NP, Alkire BC, Roy N, et al. Third delay in traumatic brain injury: time to management as a predictor of mortality. J Neurosurg 2020;132:289–95.