# Neurotrauma care in Ethiopia: Building for the future

# Tsegazeab Laeke Teklemariam

Thesis for the degree of Philosophiae Doctor (PhD) University of Bergen, Norway 2023



UNIVERSITY OF BERGEN

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# List of abbreviations

- AIS ASIA impairment scale
- ASDH acute subdural hematoma
- ASIA American Spinal Injury Association
- ATC Alert Trauma Center
- ATLS advanced trauma life support
- BHC burr hole craniostomy
- BLH -- Black Lion Specialized Hospital
- CSDH chronic subdural hematoma
- CRF case report form
- CSF cerebrospinal fluid
- CT computerized tomography
- DALYs disability-adjusted life years
- DC decompressive craniectomy
- DSF depressed skull fracture
- ED emergency department
- EDH epidural hematoma
- FIENS Federation for International Education in Neurological Surgery
- GA general anesthesia
- GCS Glasgow coma scale
- GOSE Glasgow outcome score-extended
- HIC high-income country
- HUH Haukeland University Hospital
- ICD International Classification of Diseases
- ICH intracerebral hematoma
- ICP intracranial pressure
- ICU intensive care unit
- LA local anesthesia

- LMIC low- and middle-income country
- MCM Myung Sung Christian Medical Center
- MLS midline shift
- MIIH Menelik II hospital
- PBI penetrating brain injury
- PPE personal protective equipment
- RCT randomized controlled trial
- RTA road traffic accident
- SCI spinal cord injury
- ${\rm SLIC-subaxial\ injury\ classification}$
- SPSS Statistical Package for the Social Sciences
- TBI traumatic brain injury
- TDC twist drill craniostomy
- TLICS thoracolumbar injury classification and severity
- ZMH Zewditu Memorial Hospital

# Scientific environment

The research work presented here was carried out at the Division of Neurosurgery, Department of Surgery, College of Health Sciences, Addis Ababa University in Ethiopia, and at the Department of Neurosurgery, Haukeland University Hospital and Department of Clinical Medicine, University of Bergen in Norway.

I have been registered as a PhD candidate at the Department of Clinical Medicine and at the Centre for International Health, University of Bergen. I have been enrolled in the Centre for International Health Research School.

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Tsegazeab Laeke Teklemariam Addis Ababa, 2023

### **Summary**

**Background**: Neurotrauma is a major public health problem in Ethiopia, and the main aim of this thesis was to study the management of neurotrauma patients in the country. Material and methods: We used prospective (paper I, II, and IV) and retrospective (paper III) study designs and included patients from 2012 to 2017. In paper I and II, we studied 1087 surgically treated traumatic brain injury (TBI) patients in Ethiopia. In paper III, we compared 314 Ethiopian and 284 Norwegian patients operated for chronic subdural hematoma (CSDH). In paper IV, we studied 117 hospital-treated and 51 forensically examined fall victims with TBI or spinal cord injury (SCI) in Ethiopia. **Results:** In paper I, we found that the most common cause of TBI was assault, while depressed skull fracture (DSF) and epidural hematoma (EDH) were the leading injuries. Many patients suffered significant time delays, and injury severity and time to admission were inversely related. In paper II, we showed that the most frequent operations were DSF elevation and craniotomy for EDH. The complication rate was 17% and 3% of the patients were reoperated. In paper III, we found similar surgical routines in Ethiopia and Norway, but Ethiopian CSDH patients were younger, had fewer comorbidities, rarely used anticoagulants/antiplatelets, infrequently underwent postoperative imaging, and had less reoperations and medical complications. In paper IV, we found that most fall victims were injured at construction sites, and few used protective equipment. Complete SCI was common among hospitalized patients and few SCI patients were operated. TBI was the most common cause of death among forensically examined patients and most patients died at the accident scene.

**Conclusions:** The management of neurotrauma in Ethiopia was associated with significant resource limitations and substantial patient selection both before and after hospital admission. Many patients have however benefitted from the development of neurosurgical services in Ethiopia, and our studies might help to further improve the quality of care, develop cost-effective health services, identify focus areas for preventive efforts, and guide legislative programs.

## Sammendrag

**Bakgrunn:** Nevrotraumer er et stort folkehelseproblem i Etiopia, og hovedmålet med denne oppgaven var å studere behandlingen av nevrotraumepasienter i landet.

**Materiale og metoder:** Vi brukte prospektive (artikkel I, II og IV) og retrospektive (artikkel III) studiedesign og inkluderte pasienter fra 2012 til 2017. I artikkel I og II studerte vi 1087 opererte hodeskadepasienter i Etiopia. I artikkel III sammenlignet vi 314 etiopiske og 284 norske pasienter operert for kronisk subduralt hematom (KSDH). I artikkel IV studerte vi 117 sykehusbehandlede og 51 rettsmedisinsk undersøkte fallofre med hodeskade eller ryggmargsskade i Etiopia.

**Resultater:** I artikkel I fant vi at den vanligste årsaken til hodeskade var overfall, mens impresjonsbrudd og epiduralblødning var de hyppigste skadene. Mange pasienter opplevde store forsinkelser, og det var en invers sammenheng mellom skadens alvorlighet og tid til innleggelse. I artikkel II viste vi at de hyppigste operasjonene var elevasjon av impresjonsbrudd og kraniotomi for epiduralblødning. Komplikasjonsraten var 17 % og 3 % av pasientene ble reoperert. I artikkel III fant vi at kirurgisk praksis var lik i Etiopia og Norge, men etiopiske pasienter med KSDH var yngre, hadde mindre komorbiditet, brukte sjelden antikoagulasjon/platehemmer, fikk sjelden postoperativ bildediagnostikk og hadde færre reoperasjoner og medisinske komplikasjoner. I artikkel IV viste vi at de fleste fallofrene ble skadet på byggeplasser, og få brukte verneutstyr. Komplett ryggmargsskade var vanlig blant de innlagte pasientene og få pasienter med ryggmargskade ble operert. Hodeskade var den vanligste dødsårsaken blant rettsmedisinsk undersøkte fallofre og de fleste pasientene døde på ulykkesstedet.

**Konklusjoner:** Behandling av nevrotraumer i Etiopia er assosiert med betydelige ressursbegrensninger og stor pasientseleksjon både før og etter sykehusinnleggelse. Mange pasienter har imidlertid hatt nytte av utviklingen av nevrokirurgi i Etiopia, og våre studier kan bidra til å forbedre kvaliteten på omsorgen ytterligere, utvikle kostnadseffektive helsetjenester, identifisere fokusområder for forebyggende innsats og veilede lovgivningsprogrammer.

# List of papers

#### Paper I

Laeke T, Tirsit A, Kassahun A, Sahlu A, Debebe T, Yesehak B, Masresha S, Deyassa N, Moen BE, Lund-Johansen M, and Sundstrøm T. Prospective study of surgery for traumatic brain injury in Addis Ababa, Ethiopia: Trauma causes, injury types, and clinical presentation. World Neurosurg 2021 May; 149: e460-e468. Doi: 10.1016/j.wneu.2021.02.003.

#### Paper II

<u>Laeke T</u>, Tirsit A, Kassahun A, Sahlu A, Yesehak B, Getahun S, Zenebe E, Deyassa N, Moen BE, Lund-Johansen M, and Sundstrøm T. Prospective study of surgery for traumatic brain injury in Addis Ababa, Ethiopia: Surgical procedures, complications, and postoperative outcomes. World Neurosurg 2021 Jun; 150: e316-323. Doi: 10.1016/j.wneu.2021.03.004.

#### Paper III

Laeke T, Kalleklev L, Tirsit A, Moen BE, Lund-Johansen M, and Sundstrøm T. Surgical treatment and outcome of chronic subdural hematoma: A comparative study between Ethiopia and Norway. Acta Neurochir (Wien) 2023 Jan; 165: 49-59. Doi: 10.1007/s00701-022-05435-z.

#### Paper IV

<u>Laeke T</u>, Tirsit A, Moen BE, Lund-Johansen N, and Sundstrøm T. Neurotrauma from fall accidents in Ethiopia. Manuscript submitted.

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# 1. Introduction

#### **1.1. GLOBAL BURDEN OF TRAUMA**

Trauma accounts for 9% of global mortality and more people die from trauma than from tuberculosis, malaria, and HIV combined.<sup>1</sup> Three of the top five causes of death world-wide for people under the age of 30 are injury-related.<sup>2</sup> These include road traffic accidents (RTAs), homicide, and suicide. The World Health Organization (WHO) has projected that trauma will be the fifth leading cause of death for all ages combined by 2030.<sup>3,4</sup> Trauma is a major cause of death and disability in the young and productive age group, and has therefore a significant negative economic consequence for the society.<sup>5,6,2</sup> However, one can argue that trauma has not been given the attention it deserves, perhaps because it is considered an accident – a random event.<sup>7</sup>

#### **1.2. NEUROTRAUMA – A SILENT EPIDEMIC**

Neurotrauma can be defined as trauma to the head, brain, or spine. It is the most common cause of mortality and morbidity among all injury types, particularly in young adults.<sup>8</sup> More men than women are affected by neurotrauma, and this is thought to be related to risk-taking behavior. Survivors of neurotrauma often experience permanent disability resulting in many potential lost years of working life. Traumatic brain injury (TBI) is considered a 'silent epidemic' as the true incidence remains unknown.<sup>9</sup> Many cases are never diagnosed or registered, as most patients with mild TBI do not seek medical attention and many others with severe TBI succumb before hospitalization.<sup>9</sup> It has been estimated that more than ten million people sustain TBIs annually and the incidence of traumatic spinal cord injuries (SCI) is probably around 23 cases per million in the population.<sup>10,11</sup> Neurotrauma has been estimated to account for 11.8% of global disability-adjusted life years (DALYs).<sup>12,13</sup>

#### **1.3. TRAUMA IN LOW- AND MIDDLE-INCOME COUNTRIES**

Close to 90% of all trauma-related deaths and DALYs loss occur in low- and middleincome countries (LMICs).<sup>14,15</sup> While there has been a steady decrease in deaths and permanent disability from injuries in Western countries over the last decades, there has been a significant increase in LMICs.<sup>16,17</sup> This is mainly due to the rapid urbanization of cities with heavy construction work and increasing number of cars in the absence of appropriate safety measures and legislation.

Lack of organized trauma care also contributes to the high mortality rate in LMICs.<sup>18</sup> The probability of survival from equivalent injuries is lower in LMICs than in HICs.<sup>19</sup> It must also be remembered that for every death due to RTAs in Africa and other LMICs, there are 50 times more survivors with permanent disability.<sup>20</sup> With such a high burden of trauma in LMICs, the health care system is stretched beyond its capacity. Reports show, for example, that more than 50% of the hospital bed capacity in LMICs is occupied by trauma patients.<sup>21</sup>

#### 1.4. NEUROTRAUMA IN LOW- AND MIDDLE-INCOME COUNTRIES

It has been shown that neurotrauma is more prevalent in LMICs (e.g., Sub-Saharan Africa) than in HICs.<sup>22</sup> The population in LMICs is approximately three times more likely to sustain TBIs compared to HICs.<sup>13</sup> However, region-specific data on neurotrauma from LMICs are not very reliable due a lack of structured public health surveillance.<sup>23</sup>

Despite having the major share of global neurotrauma, there are very few studies on epidemiology and neurotrauma care from LMICs in the international research literature. Tropeano et. al indicated that only 3% of all published papers on TBI were from Africa and Southeast Asia while these regions constitute 46% of the global population.<sup>24</sup> Hence, most of the evidence on treatment of neurotrauma comes from HICs. This has major implications when it comes to the adoption of guidelines and treatment recommendations given the different resource situation and epidemiological panorama in LMICs.

#### **1.5. CAUSES OF NEUROTRAUMA**

#### 1.5.1. Road traffic accidents

Worldwide, RTAs are the number one cause of death in people under 30 years of age.<sup>25</sup> It has been estimated that 1.3 million die and 50 million are injured globally each year due to RTAs.<sup>25,26</sup> It has been shown that approximately 60% of TBIs worldwide are due to RTAs.<sup>11</sup> Similarly, nearly half of SCIs are caused by RTAs.<sup>27</sup> RTAs are also among the leading causes of severe TBI and SCI in LMICs (**Figure 1**).<sup>13,28</sup>



**Figure 1.** Fatal road traffic accident in Addis Ababa, Ethiopia. This photo was taken by a visiting Norwegian neurosurgeon. Reprinted with permission from Clemens Weber.

While RTAs are declining in HICs due to a range of road safety measures, they are increasing in LMICs. Reports from Africa have shown an alarming increase in RTAs since 2000 with a 50% increase in healthy life years lost.<sup>2</sup> Africa, despite its 4% contribution to the global pool of motor vehicles, contributes to 10% of all RTAs in the world.<sup>29</sup> More than 90% of fatalities due to RTAs are from LMICs. Notably, deaths due to RTAs are expected to increase by 80% in LMICs while a 30% reduction is expected in HICs.<sup>30</sup>

Factors such as lack of seat belt and helmet usage, abundance of older vehicles with fewer safety features, and poor road standards as well as speeding and drunk driving all contribute to the increase of RTAs in LMICs. Poor enforcement of traffic laws adds to the burden. Victims of RTAs in LMICs are mainly vulnerable road users such as pedestrians and cyclists.<sup>31,32</sup>

Ethiopia is ranked second next to Kenya among East-African countries in frequency of RTAs.<sup>29</sup> It is one of the countries with the highest case fatality rates from RTAs despite its limited road coverage and relatively low number of vehicles.<sup>33,34</sup> Moreover, many people end up with severe disabilities carrying tremendous health care costs and economic losses for their families.<sup>31</sup>

#### 1.5.2. Falls

Falls are the second most common cause of unintentional injury deaths globally. Annually, almost 40 million people seek medical attention after falls and close to 700.000 people die as a result of accidents due to falls.<sup>35</sup> More than 38 million DALYs are lost annually due to falls.<sup>35</sup>

Falls mainly affect the elderly and children. Older people are at increased risk due to impaired eyesight, hearing, balance, and gait function.<sup>36</sup> Many studies on falls focus on the elderly, as global life expectancies have increased and falls are more prevalent in this age group.<sup>37</sup> About 30% of individuals older than 65 years of age sustain an accident due to falls each year, and this percentage is higher in older age groups.<sup>38</sup> Children are also more susceptible to falling as they tend to be more curious about their environment and less careful with risk-taking behavior.

Falls are the leading cause of neurotrauma in HICs, and are especially frequent among the elderly.<sup>39</sup> Their incidence among elderly citizens is steadily increasing in HICs.<sup>40</sup>



**Figure 2**. A skyscraper building under construction in Addis Ababa, Ethiopia showing the use of weak scaffolds made of wood. Photo: Tsegazeab Laeke.

It has been reported that accidents involving falls comprised the largest portion of emergency department (ED) visits in Pakistan.<sup>41</sup> In LMICs, falls are more likely to be work-related and are more common in the younger age groups.<sup>32</sup> A multi-country study from LMICs showed that more than 50% of injuries were due to falls among children.<sup>42</sup> Occupational site injuries due to falls are common and increasing in LMICs due to

shortages in occupational safety measures combined with increasing construction activity (**Figure 2**).<sup>43,44</sup> Falls among construction workers are significantly less frequent in HICs.<sup>45</sup> Moreover, farm-related fall accidents are also common in LMICs as a significant proportion of the population is involved in agriculture-related activities.<sup>46</sup> Fall accidents in Ethiopia are not given the same attention as RTAs even though they result in significant disabilities and a large number of fatalities.<sup>47</sup> A study from Ethiopia showed that falls were the most common cause of SCI.<sup>48</sup>

#### 1.5.3. Assaults

Assaults are defined as injuries caused by another person with the intention to injure or kill, by any means.<sup>49</sup> Worldwide, assaults kill around 1.5 million people each year.<sup>50</sup> They are one of the most common causes of intentional injuries and are more frequent in LMICs, especially in Sub-Saharan Africa (**Figure 3**).<sup>51-53</sup> In a Kenyan study, assaults were the leading cause of trauma.<sup>54</sup>



**Figure 3.** Men carrying sticks at a protest. Sticks are commonly used for self-protection. Reprinted with permission from Crispin Mawkideu.

Assaults are also among the most common causes of neurotrauma, especially in LMICs.<sup>55</sup> Reports from Sub-Saharan Africa have shown that assaults were the leading causes of neurotrauma.<sup>56,57</sup>

In Ethiopia, assaults are given less focus than RTAs. The burden of injuries from assaults is not well studied.<sup>47</sup> However, it has been shown that assaults were the most common indications for surgical treatment of TBI.<sup>55</sup>

#### 1.6. MAJOR INJURY TYPES AND MANAGEMENT IN ETHIOPIA

#### 1.6.1. Depressed skull fracture

A depressed skull fracture (DSF) is a fracture of the cranial vault with depression of the fractured fragment. Assault is one of the most common causes of DSF.<sup>32</sup> DSFs can be closed with an intact overlying scalp or compound with an open scalp wound.

In Ethiopia, a DSF is one of the most common TBI types leading to surgical treatment.<sup>32</sup> It is diagnosed clinically and with computerized tomography (CT) scan or conventional x-rays (**Figure 4**). Visible and palpable indentations on the skull vault can indicate a DSF. In compound DSFs, it might be possible to see fragments of bone going beneath the inner table of the adjacent bone edge. Patients can have cerebrospinal fluid (CSF) leaking through a torn dura or oozing contused brain through the scalp wound. Neurologic deficits associated with damage to the underlying brain might be involved.

Skull x-rays are inexpensive and easily available. However, these x-rays do not reveal any associated underlying hematoma or brain injury. Hence, CT scans have become the diagnostic modality of choice for all TBI patients, including those with suspected DSF.

The indications for surgical intervention of DSFs are the following:58

Closed DSF:

- Patients with neurologic deficits attributable to compression of the brain by the depressed fragment.
- Patients with significant cosmetic deformity.

Compound DSF:

- Depression of more than one cm or if the depressed fragment is going beneath the inner table of the skull vault.
- Evidence of dural tear such as pneumocephalus, oozing brain through the scalp defect, or CSF leak.
- Grossly contaminated wound with risk of wound infection.



**Figure 4.** Compound depressed skull fracture. (A) Compound DSF of the right frontal bone with the depressed fragment visible underneath the scalp wound. (B) Lateral skull x-ray of the patient showing the fracture (arrow). Photos: Tsegazeab Laeke.

Patients with a compound DSF are put on intravenous (i.v.) antibiotics immediately after presentation to the ED. Ceftriaxone is routinely started with a dose of 1 g x 2 for adults

and continued for a minimum of five days postoperatively. Patients with closed DSF are given prophylactic antibiotics at the induction of anesthesia and two doses after surgery.

A compound DSF is treated with debridement and elevation. The scalp wound is thoroughly irrigated with normal saline and any foreign bodies are removed. Patients are operated under general anesthesia (GA), and local anesthesia (LA) is infiltrated around the scalp incision. Devitalized scalp edges are trimmed out and the scalp wound is extended to completely expose the fracture. A burr hole is done close to the depressed fragment and the edges of the fractured bone are then punched out, freed, and subsequently removed. If there is a dural tear, all the edges of the tear will be exposed, and the subdural space is irrigated generously to remove any foreign bodies or devitalized brain. The dural defect is then closed with or without pericranial tissue or fascia lata depending on the size of the defect. The decision to return the fractured segment depends on the degree of comminution and contamination. The fractured segment is usually returned and left floating after thorough washing with normal saline and hydrogen peroxide. However, if there is gross contamination or infection, the bone is discarded.

#### 1.6.2. Epidural hematoma

An epidural hematoma (EDH) is a collection of blood between the dura mater and the skull. These hematomas are usually caused by a skull fracture that tears the middle meningeal artery, but venous and fracture site bleedings can also be the culprits.<sup>59</sup> EDHs are most often seen in the temporal or temporoparietal areas.<sup>59</sup> EDHs usually occur in young adults and are infrequent in the elderly due to increased dural adherence with age.<sup>60,61</sup>

In Ethiopia, an EDH is the second most common type of TBI which requires surgical treatment.<sup>62,63</sup> Approximately half of EDH patients present with a classic lucid interval after the trauma.<sup>59</sup> This is characterized by a brief loss of consciousness immediately after the injury followed by regained consciousness and then again a loss of consciousness.

Focal neurologic deficits can be present including pupillary abnormalities, hemiparesis, or seizures.

The preferred diagnostic imaging modality for EDHs is a CT scan. The hematomas typically appear as a biconvex and hyperdense collection between the brain and the skull (**Figure 5**).<sup>64</sup>



**Figure 5.** Management of epidural hematoma. (A) A non-contrast CT showing a leftsided epidural hematoma. (B) A dark clotted epidural hematoma visualized right after craniotomy. Photos: Tsegazeab Laeke.

Surgical treatment of EDH is an emergency procedure. The following treatment guidelines are used:<sup>59</sup>

- Patients with a Glasgow coma scale (GCS) score of less than nine and pupillary asymmetry should be operated as soon as possible.
- An EDH with a volume of more than 30 cm<sup>3</sup> should be evacuated regardless of the GCS score.
- Close observation is possible in patients with a GCS score of nine or more with a hematoma volume of less than 30 cm<sup>3</sup>, less than 15 mm hematoma thickness, and less

than 5 mm midline shift (MLS). Close observation includes admission to a neurosurgical center, monitoring of neurologic status, and serial CT scans.

Patients with EDHs are surgically treated with a craniotomy. Patients are given GA and LA is infiltrated around the scalp flap. Based on the location of the hematoma, scalp flaps are planned. A question mark traumatic flap is commonly used which extends from the root of the zygoma to the midline just behind the hairline. Burr holes are made using a manual drill and connected using a Gigli saw. When the hematoma has been removed, tack-up sutures are applied circumferentially to prevent hematoma recurrence. Hemostasis is secured and the bone flap is replaced. The scalp is reapproximated in layers. Perioperative care for EDHs is similar to that of DSFs.

#### 1.6.3. Acute subdural hematoma

An acute subdural hematoma (ASDH) is a collection of blood between the dura mater and the arachnoidea mater. An ASDH typically appears crescent-shaped and hyperintense on a CT scan. It can be accompanied by brain contusions, intracerebral hematomas, and/or edema. The source of bleeding is either torn bridging veins or lacerated brain parenchyma. The most common cause is a head trauma, and significant energy is usually involved with associated primary brain injury. Up to 30% of patients with a severe TBI have an ASDH.<sup>65,66</sup>

Indications for surgery of an ASDH include:65

- Hematoma thickness of more than 10 mm or an MLS of more than 5 mm regardless of GCS score.
- Hematoma thickness of less than 10 mm and an MLS of less than 5 mm with a GCS score of less than nine, and (1) a witnessed drop in GCS score by two or more points, or (2) anisocoria with a fixed dilated pupil, or (1) an intracranial pressure (ICP) of more than 20 mmHg.



**Figure 6.** Surgery of acute subdural hematoma. (A) Craniotomy flap measuring 12 x 12 cm. (B) A tense dura is exposed. (C) A clotted subdural hematoma comes out under pressure. (D) A hyperemic and swollen brain with some remaining blood overlying the frontal lobe. Photos: Tsegazeab Laeke.

In Ethiopia, patients are operated using GA and LA. A question mark scalp flap is used to expose a generous amount of the skull. A large craniotomy is undertaken measuring a minimum of  $12 \times 12 \text{ cm}$  (**Figure 6**).<sup>63</sup> The dura is opened in a cruciate or c-shaped fashion. The hematoma is evacuated, and any ongoing bleeding is identified and controlled. Expansile duraplasty is almost always done using pericranial tissue or fascia lata.

The decision to do a decompressive craniectomy (DC) is made following international consensus statements.<sup>67</sup> If there is extensive brain swelling with the brain protruding out of the outer table of the skull, the flap will be placed in the subcutaneous tissue of the abdomen. If it is possible to replace the bone flap, it will be left floating on the duraplasty. The scalp is closed in a standard manner.

#### 1.6.4. Chronic subdural hematoma

A chronic subdural hematoma (CSDH) is a collection of hemolyzed blood and blood products between the dura mater and the brain. The exact pathophysiology of CSDH is unclear. However, it is believed to be caused by tearing of bridging veins leading to a gradual accumulation of blood and blood products, and this in turn initiates an inflammatory process. After a few days, fibroblasts start membrane formation both on the surface of the brain and the inner layer of the dura.<sup>68,69</sup>

A CSDH commonly occurs in older patients with reduced brain volume and stretched bridging veins. A trivial head injury can cause a tear in these veins. Other risk factors are anticoagulant/antiplatelet use and other coagulopathies.

The incidence of CSDH worldwide is between 1.7 and 20.6 per 100.000 persons.<sup>70,71</sup> This will probably increase as the life expectancy of populations increase. Bilateral CSDHs are found in 15-25% of cases.<sup>72</sup> Patients with a CSDH usually have an insidious symptom onset with neurologic deficits and/or symptoms of increased ICP.<sup>68</sup> It is important to differentiate between this diagnosis and that of dementia.

CSDHs are typically crescent-shaped and hypodense on brain CT scans, but their appearance can be more heterogenous with both isodense and hyperdense components (Figure 7A).<sup>73</sup>



**Figure 7.** Management of chronic subdural hematoma. (A) Non-contrast enhanced CT scan showing a left-sided chronic subdural hematoma. (B) Postoperative drainage after surgical treatment. Photos: Tsegazeab Laeke.

CSDHs are one of the most common neurosurgical conditions globally, but there is no international consensus when it comes to surgical and pharmacologic treatment.<sup>74,75,68</sup> It is generally recommended that patients with symptoms that can be attributed to a CSDH should be operated.<sup>68</sup> Clinical improvement and favorable outcomes have been shown in more than 80% of surgically treated patients.<sup>76</sup>

The most widely practiced procedure is burr hole craniostomy (BHC).<sup>77</sup> Other surgical options include twist drill craniostomy (TDC) and craniotomy. A randomized controlled trial (RCT) showed that leaving a drain postoperatively significantly reduced recurrence rates and six-month mortality (**Figure 7B**).<sup>78</sup> Some studies have shown lower complication rates with surgery in LA, whereas others have shown no difference between LA and GA.<sup>79</sup>

Pharmacologic treatment with dexamethasone has been used to treat this condition. However, dexamethasone is associated with many side effects and is generally not recommended.<sup>80</sup> Tranexamic acid therapy has shown good results in CSDH patients having mild symptoms with a GCS score of 14 or 15, and in those with a recurrent CSDH.<sup>81,82</sup> Endovascular treatment options with middle meningeal artery embolization have also been explored in recent years. Tranexamic acid therapy or endovascular approaches are not used in Ethiopia.

Coagulation and platelet disorders should if possible be corrected to reduce the risk of perioperative bleeding and postoperative recurrence. It is recommended that patients taking antiplatelet therapy discontinue their treatment for at least one week.<sup>83</sup> If it is not possible to discontinue this treatment, patients should receive a platelet transfusion. Anticoagulation therapy should be stopped and reversing treatments such as vitamin K and fresh frozen plasma should be considered.<sup>68</sup>



**Figure 8.** Surgery for chronic subdural hematoma. (A) A burr hole is made using a manual drill. (B) Dark hemolyzed blood draining from the burr holes. (C) Irrigation of the subdural space with saline solution using an eight French nasogastric tube and 10 cc syringe. Photos: Tsegazeab Laeke.

In Ethiopia, a BHC is the most common procedure (**Figure 8**). It is done by making one or two burr holes over the thickest part of the hematoma. The dura is then cauterized and opened in a cruciate manner. The hemolyzed blood is allowed to pour out and the subdural space is irrigated with saline solution. An eight or 10 French nasogastric tube is usually

used for subdural irrigation. When the output becomes clear, a drain is left in the subdural or subgaleal space. A BHC is done under GA or LA.<sup>79,84-86</sup> In Ethiopia, LA is routinely used unless patients are agitated or otherwise difficult to manage with light sedation.

A twist drill craniostomy (TDC) is considered minimally invasive and is a short procedure. It involves drilling a small burr hole and then applying a closed system for drainage of the hematoma. It can be done at the bed side in LA. It is typically considered for elderly patients with multiple comorbidities.<sup>68</sup>

A craniotomy is more invasive and usually requires GA. This procedure is typically reserved for CSDHs with acute components or organized hematomas with multiple thick membranes that are difficult to evacuate through a burr hole.<sup>68,87,88</sup> Small craniotomies are preferred to large craniotomies.

#### **1.7. CHALLENGES IN LOW- AND MIDDLE-INCOME COUNTRIES**

Neurotrauma care in LMICs are faced with several hurdles including significant resource limitations, lack of well-developed trauma management systems, and a shortage of trained medical personnel.

#### 1.7.1. Prehospital care

It has been estimated that more than 40% of deaths from injuries could be prevented by provision of adequate prehospital care.<sup>89</sup> Prehospital care is one of the most important parts of the neurotrauma chain of care. Getting lifesaving care at the scene of the accident and swift transportation to definitive care can significantly reduce secondary injuries to the nervous system. Prehospital care in LMICs is, however, at its nascent stage.

Approximately 80% of trauma deaths in LMICs have been reported to occur before hospital admission. A study comparing prehospital mortality rates between high- and low-income settings showed a huge difference; 51% in Ghana and 21% in the US.<sup>90</sup>

Well-developed emergency medical systems are generally not available in LMICs. Less than 1% of the total population in LMICs have access to emergency medical transportations.<sup>91</sup> Moreover, the available ambulances are mostly used for interhospital transfers and they are not well equipped with life support equipment or appropriately trained personnel.<sup>62</sup> Interestingly, it has been reported that only 10% of TBI patients were transported by ambulances from the scene of the accident.<sup>62</sup> In addition, as many as 35% of patients brought in by ambulances had one or more vital sign derangements.

Poor infrastructure such as lack of adequate road networks and suboptimal road conditions hinder the provision of prehospital care,<sup>92</sup> and contribute to further delays in health care access. Studies have also shown that trauma patients are often first brought to centers without emergency services and/or the required expertise, which also exacerbates the delay to definitive treatment.<sup>92</sup>

#### 1.7.2. In-hospital care

Neurosurgical care for neurotrauma patients is challenged by several factors.<sup>93</sup> There is a significant shortage of trained neurosurgeons in LMICs. Thus, very few hospitals can actually properly treat patients. To cover the demand for neurotrauma treatment, it has been recommended that there should be at least one neurosurgeon per 200.000 inhabitants.<sup>94</sup> However, LMICs and especially the countries in Sub-Saharan Africa have a long way to go before they can attain even those numbers.

As mentioned, hospitals that provide neurosurgical care are scarce in LMICs due to missing infrastructure and treatment costs.<sup>93</sup> Neurotrauma patients often travel a long way to get treatment, and usually present later than the recommended four hours.<sup>95</sup> Even in hospitals that provide neurosurgical care, infrastructure challenges hamper timely treatment and surgical interventions. A report by Servadei and colleagues revealed that only 35% of hospitals in Sub-Saharan Africa had a constant supply of electricity and only 40% of surgical hospitals in Eastern Africa had a supply of oxygen.<sup>96</sup>

Neurosurgical services in the hospitals are also challenged by the shortage of surgical equipment. Appropriate surgical instruments are typically unavailable, and this results in long procedure times. Moreover, there are few intensive care units (ICU) that can provide adequate care for patients with severe neurotrauma. A recent review on intensive care services in Ethiopia showed that there were only 324 ICU beds for a population of 114 million (0.3 ICU beds per 100.000 inhabitants).<sup>97</sup> A quarter of the ICU bed capacity and half of the critical care physicians were found in the capital, Addis Ababa, underlining the disproportionate distribution of ICU services.

Access to neuroimaging modalities in LMICs is limited resulting in underdiagnosis of neurosurgical conditions, including neurotrauma.<sup>98</sup> Moreover, the long ques at imaging facilities contribute to a significant delay in diagnostics. The high cost of imaging modalities is also a limiting factor, further hindering patients from obtaining a timely diagnosis.

#### 1.7.3. Rehabilitation and follow-up

Patients with neurotrauma benefit from rehabilitation. Early physiotherapy facilitates functional recovery. However, in LMICs, rehabilitation needs are largely unmet even though this is deemed to be an integral part of the universal health coverage. Families of neurotrauma victims are primarily responsible for the rehabilitative care of their loved ones after a few days of training in the hospital by responsible nurses.<sup>99,100</sup>

Patients are usually lost to follow-up, mainly due to infrastructure challenges. Many patients come from afar and transportation is difficult and costly. Moreover, phone call follow-ups are challenging as network coverage is limited in many places and phone numbers are often changed.<sup>99</sup>

#### **1.8. NEUROTRAUMA IN ETHIOPIA**

Ethiopia has the second largest population in Africa with nearly 120 million inhabitants.<sup>101</sup> It is a country of the young, as 70% of the population is under 30 years of

age.<sup>102</sup> Trauma is the most common cause of death among this population group,<sup>103</sup> and this is a significant challenge to the Ethiopian society, not least because it affects many people in the most productive segment of the population.

Ethiopia is one of the African countries with the highest motorization and urbanization rates. However, it also has poor road and occupational safety measures. Consequently, there is a high incidence of RTAs and falls. The leading causes of major trauma in Ethiopia are RTAs, falls, and violence.

Neurotrauma is a common cause of death and permanent disability among injury victims in Ethiopia. Hospital-based studies have indicated that TBI was the leading cause of injury-related mortality and the most common indication for neurosurgery.<sup>104,105</sup> A metaanalysis also showed a high prevalence of TBI in Ethiopia; 20% of all trauma patients had a TBI.<sup>106</sup>

Ethiopia shares all the challenges faced by other LMICs in treating patients with neurotrauma. Prehospital care is not well developed. Acute care for neurotrauma patients is characterized by significant transport and treatment delays.<sup>95</sup> As a result of the delay in getting timely neurosurgical evaluation and treatment, many severely injured patients succumb before reaching definitive care.

Trauma victims in the greater Addis Ababa area are usually brought to the hospitals by taxis.<sup>62</sup> One study showed that only 10% of TBI patients were brought in by an ambulance from the scene of the accident.<sup>62</sup> As mentioned earlier, most available ambulances are used for interhospital transfers rather than transporting patients from the accident sites to hospitals. In addition, the ambulances are not well equipped and trained paramedics are lacking.

When neurotrauma patients reach the local hospitals out in the districts, they can be treated for life-threatening extracranial conditions. This primarily includes securing the airways, breathing, and circulation according to the advanced trauma life support (ATLS) guidelines. However, treatment for neurosurgical emergencies is only given in a few hospitals, and it is often necessary to transfer patients for this kind of care, causing further treatment delays.<sup>63</sup>

#### **1.9. THE BEGINNINGS OF NEUROSURGERY IN ETHIOPIA**

Provision of care for neurotrauma patients is strongly related to the growth of neurosurgery in Ethiopia. Dr. Chaba, a Bulgarian neurosurgical resident, started working at Black Lion Specialized Hospital (BLH) in 1970.<sup>107</sup> He primarily operated patients with TBI and SCI. He also diagnosed intracranial tumors using carotid angiography and operated several tumor patients. He was later joined by Prof. Woldeyes, who is regarded as the father of surgery in Ethiopia.

Modern neurosurgery in Ethiopia started in the beginning of the 1990s when two neurosurgeons, Drs. Munie and Gedlie, came back after completing their training in the United Kingdom and Cuba in 1990 and 1991, respectively.<sup>98,107</sup> Drs. Munie and Gedlie then started working at BLH serving the entire nation. They were overwhelmed by the workload and the significant resource limitations. They were assisted by general surgery residents. At this time, trauma care in Ethiopia was severely hampered by meager resources and there was no possibility of intensive care treatment for critically injured patients. Ethiopian neurosurgery was thus focused on service provision until 2006 at which time the neurosurgical training program was started.

#### **1.10. THE ETHIOPIAN NEUROSURGICAL TRAINING PROGRAM**

The Ethiopian neurosurgical training program was started in 2006 with the help of Haukeland University Hospital (HUH) in Bergen, Norway.<sup>107</sup> The goal of the program was to develop a sustainable neurosurgical service in Ethiopia. The training program received approximately 18.5 million NOK in funding and the main sponsor was the Norwegian Peace Corps. The collaboration between the two institutions involved a sixmonth rotation for neurosurgical trainees at HUH. Moreover, volunteer neurosurgeons

from Norway dedicated their time to stay and teach in Addis Ababa. Purchase of surgical equipment was also supported by HUH. Volunteer neurosurgeons from the Federation for International Education in Neurological Surgery (FIENS) were also instrumental in teaching and service coverage.

The first three graduates from the neurosurgical training program were general surgeons, and they finished their three-year training in 2010-2011. The program thereafter began enrolling general practitioners for a five-year training program in neurosurgery. Candidates were expected to complete one year of general surgery rotation to provide exposure to common surgical emergencies. Other rotations included neurology, anesthesia, neuroradiology, and plastic surgery. At the end of their training program, candidates had to sit for an exam, defend their research project, and submit their logbooks. The training program was started at BLH and Myung Sung Christian Medical Center (MCM). It subsequently expanded to Zewditu Memorial Hospital (ZMH), and Alert Trauma Center (ATC; **Figure 9**).



**Figure 9.** Neurosurgical training hospitals in Addis Ababa, Ethiopia. (A) Black Lion Specialized Hospital (BLH). (B) MyungSung Christian Medical Center (MCM). (C) Zewditu Memorial Hospital (ZMH). (D) Alert Trauma Center (ATC). Photos: Tsegazeab Laeke.

Since 2010, the training program has expanded significantly. The neurosurgical service coverage has also dramatically improved.<sup>107</sup> Abroad referrals have gone markedly down and it has become possible to do advanced procedures such as skull base surgeries.<sup>108</sup>

As of 2022, the training program has produced 64 locally trained neurosurgeons (**Figure 10**). The number of neurosurgeons and residents are growing at a rate of 20% and 26%, respectively.<sup>98</sup> In recent years, an increasing number of women have entered neurosurgery. The density of neurosurgeons per 100.000 population is now 0.05 given a population of 120 million.<sup>101</sup> However, this figure still represents an insufficient number of neurosurgeons in Ethiopia. Corley and colleagues recommended a density of 0.5 neurosurgeons per 100.000 population, and this was only to address neurotrauma in LMICs.<sup>94</sup>



**Figure 10.** Ethiopian neurosurgical workforce. Reprinted from Asfaw and colleagues<sup>98</sup> with permission from Elsevier.

It is positive that Ethiopian neurosurgery is growing rapidly, and that access to neurosurgical services has improved dramatically. Recently, two more training centers were opened at St. Paul's Hospital, Addis Ababa, and at Ayder Hospital, Mekele by
neurosurgeons who completed their training at Addis Ababa University. There are now 20 centers in 12 cities with neurosurgical services, all located in urban areas (**Figure 11**).<sup>98</sup> More than 2000 neurosurgical procedures are currently done each year. The research activity of Ethiopian neurosurgeons has also increased significantly after the start of the training program and with the increasing number of neurosurgeons.<sup>98</sup> A key issue going forward is to stimulate more research and formal research training (e.g., PhD), particularly within the most prevalent disease conditions, such as neurotrauma.



**Figure 11.** Neurosurgical centers in Ethiopia. The map presents the center with the highest World Federation of Neurosurgical Societies (WFNS) level in each location. Reprinted from Asfaw and colleagues<sup>98</sup> with permission from Elsevier.

# 1.11. THE ETHIOPIAN NEUROSURGICAL OUTCOME MONITORING DATABASE

The prospective Ethiopian neurosurgical outcome monitoring database was initiated in 2012 to monitor the quantity and quality of the neurosurgical services. The database included all operated patients at the four hospitals that were affiliated with the Division of Neurosurgery, Department of Surgery, College of Health Sciences, Addis Ababa University (BLH, MCM, ZMH, and ATC). Most neurotrauma patients included in the studies of this thesis were treated at BLH and MCM. The other centers, ZMH and ATC, first started treating TBI patients in 2015, and were not fully operational before 2016.

These four training hospitals are the major referral hospitals for the entire country. They have 24-hour emergency neurosurgical services with intensive care facilities. Attending neurosurgeons and residents are responsible for the neurosurgical treatment of the patients.

The database contains high-quality and systematic patient data on clinical status at admission, diagnosis, imaging, procedures, complications, length of stay, and outcome. Data was collected by residents using case report forms (CRF) and checked for completeness and accuracy during daily morning meetings and ward rounds. The CRFs were then collected and given to a data clerk, who registered data in the Statistical Package for the Social Sciences, version 21 (SPSS-v.21).

#### 1.12. STANDARD OF CARE FOR NEUROTRAUMA PATIENTS IN ETHIOPIA

This section describes the standard of care provided to neurotrauma patients in the major hospitals providing neurosurgical care in Ethiopia. Related issues are also covered in chapters 1.6 and 1.7.

#### 1.12.1. Traumatic brain injury

In the ED, patients are assessed by emergency physicians and interns. Life-threatening injuries are treated according to the ATLS guidelines.<sup>109</sup> All patients with TBI are

managed with head elevation and analgesics. They are kept normotensive and hypoxemia is avoided. Any scalp lacerations or other wounds are cleaned and stitched to control bleeding and prevent infection. Neurosurgical residents evaluate the patients, and the treatment plan is decided in consultation with the attending neurosurgeon on call.

If a patient has a mild TBI (GCS score 14-15), a CT scan is ordered following the Canadian head CT rule.<sup>110</sup> Patients without any indication for a CT scan are usually observed for four hours, informed about possible danger signs, and then sent home. A CT scan is done for all moderate (GCS score 9-13) or severe (GCS score 3-8) TBI patients. Patients who display signs of herniation such as anisocoria or hemiparesis are given mannitol (1 g/kg i.v.) before the CT scan. If mannitol is not available, furosemide (40 mg i.v.) is given. Severe TBI patients are intubated in the ED and put on a mechanical ventilator if available. They are then admitted to the ICU while moderate TBI patients are admitted to the wards. All patients are followed using a standardized monitoring chart, which includes vital signs, GCS score, paresis, seizure activity, and pupillary size and reactivity. If patients deteriorate clinically, a new CT scan is performed. None of the neurosurgical centers have ICP monitoring or other neuromonitoring devices.

Patients with a GCS score of less than five and/or abnormal pupillary findings are generally considered non-salvageable and not admitted to the ICU. ICU resources are shared between surgical and medical specialties at all four hospitals, and the limited availability requires tough prioritization. During the study period, there were 6, 8, 3, and 3 ICU beds, and 4, 8, 1, and 2 mechanical ventilators at BLH, MCM, ZMH, and ATC, respectively.

#### 1.12.2. Spinal cord injury

SCI patients are assessed and managed in the ED according to the ATLS guidelines, including the use of a cervical collar.<sup>109</sup> A thorough neurological evaluation is done. The spine is exposed by using log roll maneuver. All unconscious patients and patients with point tenderness along the spine, deformity of the spine, paresis of the limbs, sensory

deficit, or urinary or bowel incontinence are immobilized on stretchers (back boards are usually missing). Neurosurgical residents assess the patients according to the American Spinal Injury Association (ASIA) Impairment Scale (AIS).<sup>111</sup>

A radiological evaluation is done once the patients are stabilized. During the study period, the initial examination included antero-posterior and lateral x-rays. If the x-rays showed the spine well, treatment would be planned accordingly. If not, a CT scan was ordered. A CT scan was not the first line radiologic investigation due to cost issues. However, there has been a tendency to order more CT scans over time. MRI of the spine is typically considered in the absence of abnormalities on x-rays or CT scans despite the presence of neurologic deficits. However, the use is limited because of the involved expenses and limited availability in Ethiopia.

Patients with incomplete SCI are given priority for treatment due to the scarcity of spinal surgical implants. Complete upper cervical SCI patients with respiratory insufficiency are generally not considered salvageable, and therefore not intubated and put on mechanical ventilators.

Surgical treatment of cervical injuries is generally considered if the subaxial injury classification (SLIC) score is five or more.<sup>60</sup> Patients with incomplete SCIs and subaxial cervical injuries with fracture dislocation are first put on cervical traction to reduce the dislocation. An MRI is considered before traction if patients are unconscious or otherwise difficult to evaluate neurologically.<sup>112</sup> Cervical traction is deferred in patients with upper cervical injuries.<sup>60</sup> The degree of reduction is followed by control x-rays, and the weight is increased if acceptable reduction is not achieved.

Surgical treatment of thoracolumbar injuries is generally considered if the thoracolumbar injury classification and severity (TLICS) score is five or more.<sup>113</sup> Pedicle screw fixation is the standard surgical approach. Control x-rays are taken after the surgery.

Even though many patients present with SLIC or TLICS scores indicative of surgical treatment, they are not operated after careful considerations of survivability, rehabilitation potential, and availability of surgical resources.

Patients who are not operated are recommended immobilization for six weeks to facilitate healing. Patients with cervical injuries are fitted with collars and those with thoracolumbar injuries are put on braces. Incontinent patients are counselled to change their catheters every two or three weeks. Patients are generally followed with clinical controls at two and four weeks, and control x-rays at six weeks.

## 2. Rationale for the study

Close to 90% of all trauma-related deaths occur in LMICs and many survivors have permanent and severe disabilities.<sup>15,114</sup> Neurotrauma is a major cause of death and disability after trauma, and its treatment is demanding and expensive.<sup>115</sup> Many families and societies are faced with tremendous challenges related to treatment costs, loss of productive life years, rehabilitation, and caregiving. Although most neurotrauma cases occur in LMICs, studies from these regions are few, the epidemiology is not well known, and treatment recommendations are typically based on literature from HICs with vastly different resource situations.<sup>24,116</sup>

Ethiopia is a low-income country, and the country has limited resources for surgical care as well as prevention. A program for neurosurgical development has started in Ethiopia, but more knowledge about the patients, injury panorama, treatment standards, and patient outcomes are needed. We believe it is essential to have a better understanding of these factors ("*building for the future*") to be able to propose prevention strategies, discuss resource needs and allocations, and contribute to more tailored patient care. We further believe that our studies will not only be useful for Ethiopian health care, but also the country *per se*, as they address a major public health problem among the most productive segment of the population.

In paper I, the rationale was to provide fundamental data on epidemiology and logistics to facilitate development of preventive measures and improved access of neurosurgical care for TBI patients.

In paper II, the rationale was to identify key factors associated with patient outcome to improve the quality of care and help develop cost-effective neurosurgical care.

In paper III, the rationale was to provide data on a highly prevalent neurosurgical condition and investigate differences between a high-income setting and low-income

setting. A thorough understanding of outcome determinants and limitations can aid development of better patient care in both settings.

In paper IV, we focused on fall injuries in Ethiopia. The rationale here was to investigate a leading cause of neurotrauma to guide prevention strategies.

# 3. Aims of the study

The overall aim of this thesis was to study neurotrauma patients and their neurosurgical management in Ethiopia.

The main aims of each study were:

### Paper I

To describe demographics, trauma causes, injury types, clinical presentation, and logistics for surgically treated TBI patients in Ethiopia.

## Paper II

To assess surgical management, complications, and outcome of surgically treated TBI patients in Ethiopia.

## Paper III

To compare demographics, management, and outcome of CSDH patients in Norway and Ethiopia.

## Paper IV

To describe fall injuries and associated TBI and SCI in Ethiopia.

# 4. Participants and methods

The study objective, population, setting, and design are summarized in Table 1.

Paper	Objective	Population	Setting	Design
Ι	To describe	Surgically treated	Hospitals: BLH,	Prospective
	demographics, trauma	TBI patients	MCM, ZMH, and	cross-
	causes, injury types,	from October	ATC in Addis	sectional
	clinical presentation,	2012 to	Ababa, Ethiopia	study
	and logistics for	December 2016	_	-
	surgically treated TBI			
	patients in Ethiopia.			
Ш	To assess surgical	Surgically treated	Hospitals: BLH,	Prospective
	management,	TBI patients	MCM, ZMH, and	cohort study
	complications, and	from October	ATC in Addis	
	outcome of surgically	2012 to	Ababa, Ethiopia	
	treated TBI patients in	December 2016		
	Ethiopia.			
III	To compare	Surgically treated	Hospitals: BLH,	Retrospective
	demographics,	CSDH patients	MCM, ZMH, and	comparison
	management, and	from 2013 to	ATC in Addis	
	outcome of CSDH	2017	Ababa, Ethiopia,	
	patients in Norway and		and HUH in	
	Ethiopia.		Bergen, Norway	
IV	To describe fall injuries	Fall victims with	Hospitals: BLH,	Prospective
	and associated TBI and	TBI or SCI	MCM, ZMH, ATC	cohort study
	SCI in Ethiopia.	treated at	and MIIH in Addis	
		hospitals, or	Ababa, Ethiopia	
		forensically		
		examined in		
		2017		

**Table 1.** Summary of objectives, population, setting, and design of the studies in this thesis. Abbreviations: TBI, traumatic brain injury; BLH, Black Lion Hospital; MCM, Myung Sung Christian Medical Center; ZMH, Zewditu Memorial Hospital; ATC, Alert Trauma Center; MIIH, Menelik II Hospital; LIC, low-income country; HIC, high-income country; CSDH, chronic subdural hematoma; HUH, Haukeland University Hospital; SCI, spinal cord injury.

#### 4.1. STUDY SETTING

Paper I and II were done at the four neurosurgical teaching hospitals in Ethiopia (BLH, MCM, ZMH, and ATC), affiliated with the Division of Neurosurgery, Department of Surgery, College of Health Sciences, Addis Ababa University. These hospitals are neurosurgical referral centers, receive patients from the entire country, and provide 24-hour emergency neurosurgical services. Neurosurgical attendings and residents are responsible for the treatment and follow-up of patients. BLH is the biggest tertiary teaching hospital in Ethiopia and the pioneer training site for many surgical specialties, neurosurgery included.

Paper III was done at BLH, MCM, ZMH, and ATC in Addis Ababa, Ethiopia, and at the Department of Neurosurgery, HUH, Bergen, Norway. HUH is the largest hospital in western Norway, the regional trauma center, and has a total catchment area of approximately 1.1 million people.

Paper IV was done at BLH, MCM, ZMH, ATC, and Menelik II hospital (MIIH), Addis Ababa, Ethiopia. The Department of Forensic Pathology at MIIH serves the entire country.

#### 4.2. STUDY POPULATION

Paper I and II included surgically treated TBI patients from October 2012 to December 2016 at BLH, MCM, ZMH, and ATC in Ethiopia. All patients were consecutively registered in the Ethiopian neurosurgical outcome monitoring database.

Paper III included surgically treated CSDH patients from 2013 to 2017 at BLH, MCM, ZMH, and ATC in Ethiopia, and at HUH in Norway.

Paper IV included fall victims in Ethiopia who were treated at BLH, MCM, ZMH, and ATC, or brought to MIIH for forensic examination in 2017.

#### 4.3. STUDY DESIGN

Paper I was a prospective cross-sectional study to investigate trauma causes, injury types, and clinical presentation of surgically treated TBI patients.

Paper II was a prospective cohort study to assess the surgical procedures, postoperative complications, and in-hospital treatment outcomes of surgically treated TBI patients.

Paper III was a retrospective study based on journal review of operated CSDH patients.

Paper IV was a prospective cohort study of fall victims who were hospitalized or forensically examined.<sup>103</sup>

#### 4.4. DATA COLLECTION

Data from the Ethiopian neurosurgical outcome monitoring database was used for papers I to III.

In paper I, we collected data on demographics, trauma causes, time of injury, time of admission, distance from injury site to the hospital, TBI severity, CT scan findings, and presence of other injuries. Trauma causes were categorized according to the International Classification of Diseases, 10<sup>th</sup> revision (ICD-10).<sup>117</sup> TBI severity was categorized as mild (GCS score 14-15), moderate (GCS score 9-13), or severe (GCS score < 9).<sup>118</sup>

In paper II, we collected data on the time of events, CT scan findings, surgical procedures, perioperative blood loss, admission and discharge GCS score, postoperative complications, and mortality.

In paper III, we collected data on admission GCS score and Markwalder's grade, demographics, trauma mechanisms, presence of comorbidity, medication history, clinical findings at admission, CT scan findings, surgical procedures, complications, and GCS score at discharge. Time of death was available via the electronic medical records for all Norwegian patients. Patients who consented underwent follow-up interviews with Glasgow outcome scale-extended (GOS-E) scoring.<sup>119</sup>

In paper IV, we collected data on demographics, fall types, injury types, injury severity, provision of prehospital care, time from injury to neurosurgical evaluation, and inhospital treatment. GCS score and AIS grade were used to classify injury severity at admission and discharge.<sup>118,120</sup> Types of falls were classified according to the ICD-10.<sup>117</sup> Falls at construction sites and use of personal protective equipment (PPE) such as helmets or ropes were also registered. SLIC and TLICS scoring were used to categorize spinal injuries.<sup>121,122</sup> Patients who consented were interviewed for GOS-E scoring and AIS grading. We also included patients who succumbed after fall accidents and were brought in for forensic examination. For these patients, we registered demographics, fall types, use of PPE, treatment, and causes of death.

#### 4.5. DATA MANAGEMENT AND ANALYSIS

A data clerk was hired to plot data from the CRFs into SPSS-v.21. The data was then cleaned and checked for missing values. All statistical analyses were performed using SPSS-v.21. A p-value of < 0.05 was considered significant.

Descriptive statistics were done using frequencies and percentages for categorical variables. Measures of central tendency (mean, median, standard deviation (SD), interquartile range (IQR), frequency, and percentage) were used to describe continuous variables. Independent Student's t-test and Mann-Whitney U test were used to compare means.

Cross tabulations were done for categorical variables to evaluate the association between variables. Predictive analysis was done using logistic regression incorporating variables that displayed significant association by chi-square cross tabulations.

In paper I, we performed binomial and multinomial logistic regression analysis to determine predictors of TBI severity using demographics, trauma mechanisms, geographical distance, and time interval between trauma and admission.

In paper II, we analyzed frequencies and percentages of the different types of surgical procedures. Logistic regression analyses were done to determine predictive factors of postoperative complications and mortality.

In paper III, we analyzed demographics using frequencies and percentages. Comparative analyses were done using chi-square test, independent Student's t-test, and Mann-Whitney U test.

In paper IV, we analyzed frequency and percentage tables to determine the most common types of falls and neurotrauma. Injury sites were dichotomized as construction and non-construction sites. The use of PPE was also described using frequencies and percentages. Differences between falls from construction sites and other types of falls were evaluated using demographics, injury severity, and time from injury to neurosurgical evaluation. Treated and deceased fall victims were compared using demographics, fall types, prehospital, and in-hospital care.

#### 4.6. ETHICAL CONSIDERATIONS

Regulatory ethical approvals were obtained from the Institutional Review Board (003/16/surg), Addis Ababa University, Ethiopia, and the Regional Ethical Committee (2018/53), University of Bergen, Norway. All data retrieval, registration, and management followed national and institutional regulations and legislation. We also adhered to the Nuremberg Code (1947), the Revised Declaration of Helsinki (1975), and Convention on Human Rights and Biomedicine (1997).

There were differences in consent regulations in Ethiopia and Norway. Ethiopian patients provided a telephone number during their hospital stay (their own or a family member's),

and it was allowed to contact the patient or relatives, ask for consent, and then interview them. This legislative measure is an important substitute for incomplete official death statistics and is called *verbal autopsy*.<sup>123</sup> In Norway, for paper III, we contacted the living Norwegian patients by mail and interviewed those who consented by telephone. The decisional capacity of patients was considered prior to mail contact by review of electronic medical records.

## 5. Results

The main findings from the studies are presented here. Detailed results are presented in the respective manuscripts.

## Paper I: Prospective study of surgery for traumatic brain injury in Addis Ababa, Ethiopia: Trauma causes, injury types, and clinical presentation

We included a total of 1087 surgically treated TBI patients over a four-year period from the neurosurgical teaching hospitals in Addis Ababa. Males (91.3%) vastly outnumbered females, and females were younger than men (24.7 vs. 29.4 years of age, respectively). Only 15.5% of TBIs were classified as severe and very few TBI patients were multitraumatized (3.1%). Overall, DSF (44.9%) and EDH (39%) were the most common injury types. ASDH was the most frequent injury type among RTA victims (32.6%).

There was a median delay of 24 hours from injury to hospital admission, even though 80% of patients came from within a radius of 200 kms. There was an inverse relationship between injury severity and logistical delay; those who came in late had less severe injuries, whereas those who were brought in within six hours of injury had a median GCS score of 11. Time to admission and distance from the injury site to the hospital were significantly associated.

Assault (70%) was the most common cause of TBI, followed by RTAs and falls. Most of the assaults (80%) occurred in rural areas more than 50 kms from Addis Ababa, and half of the assaults were due to stick injuries. Victims of RTAs were more frequently from urban areas (46%), and most of them were pedestrians (73%). Fall accidents were typically caused by fall from ladders, buildings, stairs, or scaffolds.

Assault, DSF, and long delay to admission was associated with a lower risk of severe TBI. Falls, ASDH, and EDH were predictors of severe TBI.

## Paper II: Prospective study of surgery for traumatic brain injury in Addis Ababa, Ethiopia: Surgical procedures, complications, and postoperative outcomes

In this study, we used the same patient cohort as in paper I. While paper I dealt with trauma causes, injury types, and clinical presentation, paper II assessed the surgical treatment, complications, and patient outcomes.

The most frequent operations were elevation of a DSF (49.5%) and craniotomy (47.9%). EDH was the most common indication for a craniotomy (74.7%). Patients undergoing DSF elevation or craniotomy had a median length of hospital stay of four days, whereas those who underwent DC had a stay of nine days. Traumatic intracerebral hematoma (ICH) and penetrating brain injury (PBI) had the longest median hospital stays with 11 and seven days, respectively.

The postoperative complication rate after TBI surgery was 17%, and 3% of the patients were reoperated. CSF leak was the most common complication. However, the most common indication for reoperation was wound infection, and patients with wound infections had the longest median hospital stays (21 days). Patients with complications had a lower mean GCS score at discharge than those who had no complications.

The mortality rate was 8.2%. Among those who died, 46% had postoperative complications. Postoperative complications were associated with a five-fold risk of dying compared to those without complications. The highest and lowest mortality rates were found in patients with ASDHs and DSFs, respectively. Patients who died were older and admitted earlier than those who survived. The mortality rate of severe TBI patients was 42.3% and admission GCS score was strongly associated with mortality. Age, admission GCS score, and length of hospital stay were significant predictors of death.

# Paper III: Surgical treatment and outcome of chronic subdural hematoma: A comparative study between Ethiopia and Norway

Over a five-year period, we included 314 CSDH patients from Ethiopia and 284 from Norway. In both countries, three out of four patients were male, most patients had a history of trauma, fall injuries were the most common injury mechanism, most patients had a GCS score of 14-15, left-sided hematomas were most frequent, BHC in LA was the standard surgical approach, nearly all patients had postoperative drainage, and most patients had a discharge GCS score of 14-15.

Norwegian patients were older than their Ethiopian counterparts (median 75 vs. 60 years of age), had more comorbidities (77.5 vs. 30.3%), more frequently used anticoagulant/antiplatelet therapies (45.1% vs. 3.2%), more often had hemiparesis (45.4% vs. 17.8%), more frequently underwent postoperative CT scanning (99.3% vs. 5.2%), had more reoperations (10.9% vs. 6.1%), and had more medical complications (6.7% vs. 1.3%).

The mortality rate at one year postoperatively was 7% in Norway and 3.5% in Ethiopia. At the end of follow-up (> 3 years), a GOS-E score of eight (upper good recovery) was present in 46.8% of Norwegian patients and 82.9% of Ethiopian patients. Age, comorbidity, and neurological status at admission were significantly associated with mortality.

#### Paper IV: Neurotrauma from fall accidents in Ethiopia

In 2017, we included all fall victims who were hospitalized for neurotrauma at BLH, MCM, ZMH, and ATC (N=117), or forensically examined at MIIH (N=51). Male patients were vastly overrepresented in both groups.

The hospital-treated fall victims had a median age of 27 years, most frequently worked as construction workers (25.6%), and were most commonly injured at construction sites (42.7%). PPE was only used by 36% of patients who were injured at construction sites.

Most of the hospital-admitted patients (89.8%) were referred from local hospitals or health centers, only 47% received treatment before admission to the study hospitals, and many patients suffered significant temporal delays (median 24 hours). However, construction site victims were admitted earlier than other fall victims (median 6 hours vs. 48 hours).

Among the hospitalized patients, SCI was more frequent than TBI (50.4% vs. 39.3%), 10.3% of the patients had both SCI and TBI, 18.8% were multitraumatized, and 13.7% had hypoxemia or hypotension at admission. Most SCIs were AIS grade A (complete injury; 49.3%), whereas most TBIs were mild (GCS score 14-15; 55.2%). Moderate and severe TBI occurred with similar frequencies, and most SCIs were cervical (42.3%). Less than 50% of TBI patients and less than 20% of SCI patients were operated. However, most SCI patients had SLIC or TLICS scores of more than four, indicating surgical treatment.

At a median of 33 weeks, follow-up data was registered on 96% of the discharged patients (42 TBI and 62 SCI cases). In total, there were approximately twice as many deaths among TBI patients (n=15) as SCI patients (n=8). Among those who were discharged alive, 50% of TBI patients had a GOS-E score of eight (upper good recovery) and 35.5% of SCI patients had AIS grade A (complete injury). The relative frequency of SCI patients with AIS grade E (normal function) was 30.6% at follow-up compared to 18.3% at discharge.

The forensically examined patients had a median age of 40 years, most frequently worked as farmers (41.2%) or construction workers (27.5%), and were most commonly injured at construction sites (33.3%). Among the fatalities who were injured at construction sites, PPE was only used by 23.5%. Most of the deaths occurred at the accident site (90.2%), and the most common cause of death was TBI (64.7%) and SCI (27.5%).

## 6. Discussion

#### 6.1. MAIN FINDINGS

In our studies, we have presented novel data on neurosurgical care of neurotrauma patients in Ethiopia. The typical emergency case was a young male assault-victim with a mild TBI admitted 24 hours after the injury who underwent an operation for a DSF or EDH. Many patients also suffered TBI or SCI from fall accidents, and most of these occurred at construction sites with inadequate occupational safety measures. The injury panorama, significant time delays before admission, and few operations for more severely injured patients were highly influenced by a substantial patient selection both before and after hospital admission. The neurosurgical services were hampered by significant resource limitations but still benefited a large number of patients with results that were qualitatively comparable to reports from HICs.

The TBI literature is heterogenous, and there are numerous examples of studies that have reported different findings than we have, most of which are from HICs with vastly different resource situations.<sup>124,125</sup> In our opinion, this underscores the need to study your own patients, in your own location, and with your available resources. Knowing what you have to deal with and what you can do will make it easier to identify focus areas for improvement and move forward.

#### 6.2. CHARACTERISTICS OF TBI PATIENTS AND INJURY TYPES

The most common surgical cases were young males with a left-sided DSF and/or EDH, and high GCS scores, who came in a day after an assault from rural areas outside of Addis Ababa. This pattern of demographics and injuries could largely be explained by sociocultural factors, prehospital treatment and logistics, and hospital prioritizations.

Among the various types of assaults, stick injuries were found to be the most common. Most Ethiopians live in rural areas<sup>126</sup>, and it is here commonplace to carry sticks for selfprotection and support. Whenever there is fighting, most often between men, they hit each other with these sticks. They frequently strike each other's heads, and as most people are right-handed, most injuries are seen on the left side of the head. These focal impacts typically result in superficial wounds and/or cranial fractures with or without associated EDHs. Stick injuries are most frequently located over the cranial vault, possibly affecting more minor branches of the middle meningeal artery and are therefore less likely accompanied by large EDHs. These injuries are also of low energy and less prone to affect more global cerebral functions, such as consciousness. Hence, most patients are awake with favorable GCS scores. Studies from Tanzania and Uganda have also shown that assault victims were more likely to receive surgery than those who sustained RTAs.<sup>127,128</sup> In a report from Cambodia, comparable to our study, Peeters and colleagues also found a high frequency of DSFs.<sup>129</sup>

#### 6.3. CONTINUUM OF CARE FOR NEUROTRAUMA PATIENTS

Our findings showed a delay in hospital presentation of TBI patients which was longer than reported in other studies.<sup>130-132</sup> In Ethiopia, prehospital treatment and ambulance services are largely missing, local hospitals are poorly equipped and lack necessary training, and road standards are generally poor.<sup>133</sup> Many critically injured patients therefore succumb before reaching definitive care at the neurosurgical centers in Addis Ababa.

In addition to the prehospital time delays reported in paper I, we also found significant delays from admission to surgery in paper II. Similar findings have also been reported in a Ugandan study and was associated with higher mortality rates.<sup>134,135</sup> This inhouse delay was mainly caused by significant resource limitations in the hospitals such as scarcity of ICU beds and mechanical ventilators,<sup>97</sup> making it necessary to prioritize patients with better prognoses. ICU admission and surgical treatment was, and still is, therefore prioritized for patients with a GCS score of five or better, and normal pupillary findings.

Our findings reflect a substantial selection of patients throughout the entire chain of care. Many severely injured patients either die at the scene or during transport. Moreover, surgery is withheld for many patients in poor condition that reach the neurosurgical centers. In a previous study on severe TBI admitted to BLH, more than half of the patients died in the ED, and less than two out of three survivors were operated.<sup>62</sup>

It would have been interesting to have more data on secondary insults like hypoxemia and hypotension among neurotrauma patients both in the prehospital and in-hospital setting in paper I-II, but these data were to a large extent nonexistent. In paper IV, we registered hypotension and hypoxemia at admission. However, these factors are key outcome determinants for patients and would need to be addressed more specifically going forward.

Moreover, it would be better to have more comprehensive follow-up data, especially after discharge where many patients are lost to follow-up and where rehabilitation is left to the families. This limited follow-up in Ethiopia was evident across papers I-III. In the retrospective paper III, where CSDH patients were contacted for a follow-up interview, we only obtained data on half of them. However, in the prospective paper IV, we obtained follow-up data on 96% of the patients, demonstrating that it is possible to get more comprehensive outcome data. Moreover, there is no national death registry in Ethiopia and valid mortality data was therefore difficult to obtain; we only had access to a selected group of patients reached by phone calls. Consequently, there were major uncertainties related to follow-up data on Ethiopian patients. In Norway, on the other hand, it was possible to obtain complete mortality data via the national death registry.

#### 6.4. SURGICAL TREATMENT AND OUTCOME OF TBI PATIENTS

Given the significant patient selection with DSF and EDH as the most frequent diagnoses, the most common operations were elevation of DSFs and craniotomies for EDHs. Most patients were in a relatively good clinical condition at admission with short hospital stays, few complications, and good outcomes. Our findings contrasted results from many other surgical series in the international literature, many of which from HICs, where implantation of ICP probes, evacuation of ASDH, and DC were more frequent.<sup>66,136-138</sup>

The overall postoperative complication rate was 17% and only 3% of patients were reoperated. These numbers were lower than anticipated given the substantial time delays and resource limitations. Patients who underwent DSF elevation had a 12.8% complication rate. For these patients, routine antibiotic prophylaxis probably contributed to a lower frequency of wound infections, and lack of glue and dural substitutes likely contributed to a higher frequency of CSF leaks, than previously reported.<sup>139,140</sup>

The overall mortality rate was 8.2%; this was similar to a Ugandan study, but lower than a Malawian study.<sup>130,136</sup> Patients with mild to moderate TBI usually had good discharge outcomes, akin to previous reports from LMICs.<sup>141</sup> However, patients with severe TBI had a mortality rate of 42.3%, higher than previously reported.<sup>142</sup> Unfavorable outcomes were associated with advanced age, short time to admission, low GCS score at admission, ASDH, complications, and long hospital stays. A low GCS score at admission was a strong predictor of mortality, as reported in numerous studies. Mortality rates of severe TBI have also been found to be higher in LMICs as compared to HICs.<sup>136,141</sup> This is probably related to lack of timely treatment, ICU care, neuromonitoring, and rehabilitation, but also prioritization where treatment is withheld or stopped for patients in poor clinical condition (e.g., GCS score 3-4 and/or one or two fixed and dilated pupils).

## 6.5. SOCIODEMOGRAPHIC AND TREATMENT VARIATIONS BETWEEN HIGH- AND LOW-INCOME COUNTRIES

In paper III, we observed significant differences between Norwegian and Ethiopian CSDH patients. Norwegians were older than their Ethiopian counterparts, reflective of the higher life expectancy in Norway and other HICs, similar to previous reports.<sup>84,143,144</sup> Medical comorbidities were significantly more prevalent in the Norwegian patients, including use of anticoagulants/antiplatelets. Studies from other HICs have also showed

that a large proportion of CSDH patients take anticoagulants/antiplatelets and there is a greater tendency to prescribe such medications to elderlies in HICs.<sup>85,145</sup>

The most common surgical treatment in both countries was BHC under LA with postoperative drainage, similar to other studies.<sup>79</sup> There is no consensus on GA vs. LA for CSDH surgery, but lower complication rates are frequently reported for LA.<sup>79,146</sup> Most of the Ethiopian patients with bilateral CSDH were operated on both sides at the same time. The majority of patients in Norway received interval surgery, as also reported in a Danish study.<sup>72</sup> The decision to operate on one side depended on the size of the hematoma and the laterality of symptoms.<sup>147</sup> Duration of postoperative drainage, age of patients, and admission GCS score were not associated with hematoma recurrence, as reported previously.<sup>148,149</sup>

There were large differences in the use of postoperative CT scanning. Nearly all patients in Norway were scanned after surgery. In Ethiopia, a CT scan was only done in patients who displayed neurological deterioration. Previous studies have shown that there is limited value of postoperative CT scanning for CSDH patients with no clinical deterioration; it rather increases the financial cost, reoperations, and length of hospital stay.<sup>150,151</sup> Nevertheless, postoperative CT scanning might provide valuable educational benefits for younger neurosurgeons.

The recurrence rate in Ethiopia was lower than in Norway. This was probably related to age, anticoagulation/antiplatelet use, and postoperative CT scanning. Similar risk factors have also been reported in other studies.<sup>152,153</sup>

Taken together, despite the major differences between the two countries, there were major similarities with respect to surgical treatment of CSDH. Norway, which might be considered a "benchmark" HIC, should probably reduce the use of postoperative CT scanning and the use of interval surgery in bilateral CSDHs. Ethiopia would probably

benefit from more comprehensive outcome data, especially death statistics, and followup data on patients in need of rehabilitation.

#### 6.6. FALL-RELATED NEUROTRAUMA

Fall accidents are one of the leading causes of neurotrauma. Our findings showed that construction site falls were the most common fall types among patients treated in the study hospitals. Similar studies have also reported construction site falls to be the most common fall accidents.<sup>43,44</sup> This was related to limited use of PPE, as also demonstrated in a previous study reporting a 10-20 times higher risk of safety hazards in LMICs compared to HICs.<sup>154</sup> Other contributing factors are probably non-compliance to construction site safety measures and weak scaffolding systems primarily made of eucalyptus wood.<sup>155</sup>

Among forensically examined fall victims, TBI was more than twice as common as SCI, and the vast majority of patients died at the accident site. Fall accidents at construction sites were also most common among those who were forensically examined. These patients were older than those who were admitted to the hospitals, most of them were farmers from the countryside, and fewer of them used PPE. Comparable findings were reported in a previous study, where they also found that rural fall victims were older than urban fall victims.<sup>156</sup>

There were significant time delays between the fall accident and hospital admission. As reported in paper I, it is likely that poorly developed prehospital systems and limited access to hospitals with neurosurgical services played key roles as barriers to definitive care.<sup>157</sup> Fall victims from construction sites were brought in faster than others, probably because these accidents more often occurred in urban areas and were observed by colleagues. A shorter prehospital delay and increased probability of survival might have contributed to a larger fraction of construction site falls in our study.

SCI was more common than TBI among hospital-treated patients. Almost 50% of SCI patients had AIS grade A (complete injury) and more than 20% of TBI patients had a GCS score of less than nine (severe injury). The high number of complete SCIs in fall accidents from heights is similar to a previous report, whereas the high frequency of severe TBIs was more than previously reported.<sup>62,158</sup> Concordant with other reports from Sub-Saharan Africa, more than half of the severe TBI patients succumbed.<sup>62,136</sup>

Most SCI patients had SLIC or TLICS scores of more than four, which are indicative of surgical treatment, but less than one in five SCI patients were operated. As previously discussed in papers I-II, this was likely related to patient selection factors such as survivability and rehabilitation potential, as well as availability of ICU and surgical resources. Notably, most SCI patients were injured at the cervical level, and these injuries were difficult to treat and carried a dismal prognosis.

The follow-up rate of 96% was relatively unique in a LMIC context, as previously discussed. Nearly all SCI patients with AIS grade A (complete injury) were unchanged at discharge, but approximately one in four had a better AIS grade at follow-up. Most TBI patients did well with a GOS-E score of 7-8 (lower to upper good recovery), but there were twice as many deaths among TBI patients compared to SCI patients.

In summary, fall accidents with SCI and TBI most frequently occurred at construction sites. More use of PPE and other safety measures at construction sites are warranted.

#### 6.7. METHODOLOGICAL CONSIDERATIONS

All our studies were hospital-based studies, primarily at the major hospitals that provide neurotrauma care in the country, and all of these were located in Addis Ababa. This might impact the generalizability and representativeness of our findings to the larger population of Ethiopia. The studies provided important information on the disease panorama and treatment outcome of neurotrauma patients, but with significant limitations on mortality data because of missing prehospital death rates and incomplete follow-up data after discharge.

The neurosurgical outcome monitoring database in the study hospitals was the primary data source for papers I-III. Data collection using paper-based CRFs was challenging, and frequent quality assurance was necessary to secure completeness and accuracy. The clinical status of patients was evaluated using internationally accepted and validated scales such as the GCS score, GOS-E score, and AIS grade. This enables more objective comparison to other studies both in our setting and other similar settings.

The discharge outcome was prospectively registered as GCS score in the database. This was done to simplify registration and decrease data variability. However, this variable is not well suited for outcome assessment and has later been replaced by GOS-E scoring. For papers III-IV and ongoing projects, we also included more longitudinal outcome data.

#### **6.8. STUDY POPULATION**

Papers I-II included all surgically treated TBI patients during the study period. We believe that the sample size was adequate and representative for the greater Addis region, as it included patients from all the teaching hospitals. The hospitals did receive patients from all corners of the country, but this representation was highly biased due to significant prehospital selection factors (e.g., severity, survivability). Moreover, the availability and quality of neurosurgical services are not equally distributed across the country, and our results are probably not representative for all regions and hospitals.

The number of study participants in paper III were comparable in Norway and Ethiopia and an adequate number of patients were included in the study. It was possible to do comparative analyses of patient characteristics and treatment variations between the two settings. As previously discussed, however, it was impossible to trace all patients after discharge to get follow-up data on clinical status and mortality. In paper IV, it was possible to include details of forensic results on all prehospital fall victims over a one-year period and compare the demographic characteristics and fall types of these patients with the hospitalized patients.

## 7. Conclusions

#### Paper I

The surgical management of TBI in Addis Ababa was dominated by assault victims with mild to moderate head injuries. These findings were linked to significant shortcomings in prehospital (e.g., time delays) and in-hospital management (e.g., salvageability assessment) resulting in significant patient selection bias.

#### Paper II

A large number of patients in the greater Addis region benefited from neurosurgical treatment, qualitatively comparable to reports from HICs. As indicated above, several factors associated with patient selection were also highly relevant for surgical activity and patient outcomes.

### Paper III

The surgical management in Ethiopia and Norway was similar, but Norwegian patients had poorer outcomes. This was related to differences in age distribution, comorbidities, medication use, and complication rates.

#### Paper IV

Construction site falls were the most common fall accidents causing TBI and SCI in Ethiopia. Many patients were severely injured or died, and experienced significant delays along the entire continuum of care. Workplace safety was a major concern, evident by limited used of PPE.

## 8. Future perspectives

#### 8.1. SURGICAL CARE FOR NEUROTRAUMA IN ETHIOPIA

Neurotrauma is a major public health problem in Ethiopia, and it is important to highlight the unique epidemiological and therapeutic challenges. Many young people die or suffer significant treatment delays due to limitations throughout the entire chain of care. Prehospital services are largely missing, local hospitals are poorly equipped and trained, neurosurgical centers and ICU departments have limited capacity, rehabilitation is usually left to the families, and follow-up and death statistics are fragmented and incomplete. Challenges with infrastructure, legislation, safety standards, and public awareness add to this burden.

There are several takeaways from our studies, which can help to improve the quality of neurosurgical care, further develop cost-effective health services, identify focus areas for preventive efforts, and guide legislative programs. Many obstacles are not unique to the neurosurgical domain, and prioritizations and solutions should be discussed between medical experts, health care leaders, and local and governmental officials.

Improved access to ambulances with personnel trained in emergency medicine could benefit many injured people. Furthermore, treatment delays and insufficient acute management can be addressed by more systematic referral systems between local hospitals and neurosurgical departments, development of telemedicine programs, increased radiological accessibility, and neurosurgical outreach and training programs.

Neurosurgical centers should maintain a strong focus on education and research, quality assurance projects, development of locally tailored practice routines, and improvement of ICU capacity. Further ahead, with increasing opportunities to treat more and more severely injured patients, more comprehensive neuromonitoring should be considered.

Finally, short- and long-term rehabilitation should become a more integrated part of the treatment.

Specifically, it might be beneficial to develop prevention strategies against stick injuries in rural Ethiopia. Public awareness campaigns and prohibition of stick use in public places might be ways to reduce the high frequency of these injuries. Moreover, given the high frequency of construction site falls, more focus should be directed at the use of PPE and other safety measures, such as better scaffolding, safeguards, training, safety rules, legislation, and oversight.

Despite numerous challenges to neurotrauma care in Ethiopia, many TBI and SCI patients benefit from neurosurgical treatment. As we have demonstrated in our studies, the clinical competency and surgical results are generally good, and bear comparison to a large number of international reports, including reports from other LMICs and HICs.

#### 8.2. ADDRESSING GAPS IN NEUROTRAUMA RESEARCH

Neurotrauma management is an essential aspect of healthcare in Ethiopia, and the country has made significant progress in recent years. However, there are still gaps in research that need to be addressed to improve the management of neurotrauma patients in the country. Ethiopian neurosurgeons and health care authorities should also use research data and their expanding reach to influence policy makers, stakeholders, and advocacy groups in developing prevention strategies, new legislation, and increase neurosurgical resource allocation.

One of the main challenges in neurotrauma research in Ethiopia is the lack of data. There is a need to establish a comprehensive database of neurotrauma patients, including information on the mechanism of injury, severity, treatment, and outcomes. This data can be used to identify trends and patterns in neurotrauma management and inform the development of evidence-based guidelines. Such research in Ethiopia should build upon the experience from the neurosurgical teaching hospitals and expand and include more of the new neurosurgical centers that are being established across the country to improve representativeness and generalizability. For instance, the know-how acquired to build up a neurotrauma database can be shared with the new hospitals, and possibly enable the development of a national neurotrauma registry.

Another important area of research is the evaluation of the effectiveness of neurotrauma treatments in the Ethiopian context. Many of the treatments used in high-income countries may not be feasible or effective in low-resource settings like Ethiopia. Therefore, it is essential to conduct research on the efficacy of interventions that are available and feasible in Ethiopia.

Research on the long-term outcomes of neurotrauma patients is also crucial. There is a need to establish a follow-up system to track the outcomes of neurotrauma patients and identify factors that may influence their recovery. This information can be used to improve the quality of care provided to neurotrauma patients and inform the development of rehabilitation programs.

Furthermore, research on the prevention of neurotrauma is essential. Many neurotrauma cases in Ethiopia are preventable, and research on the most effective prevention strategies can help reduce the burden of neurotrauma in the country.

In conclusion, there are several gaps in neurotrauma research in Ethiopia that need to be addressed. Establishing a comprehensive database of neurotrauma patients, evaluating the effectiveness of treatments, researching long-term outcomes, and prevention strategies are some of the areas that require further research. Addressing these gaps can help improve the management of neurotrauma patients in Ethiopia and reduce the burden of neurotrauma in the country.

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10. Papers I-IV

# Paper I



# Prospective Study of Surgery for Traumatic Brain Injury in Addis Ababa, Ethiopia: Trauma Causes, Injury Types, and Clinical Presentation

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**BACKGROUND:** Traumatic brain injury (TBI) is a public health problem in Ethiopia. More knowledge about the epidemiology and neurosurgical management of TBI patients is needed to identify possible focus areas for quality improvement and preventive efforts.

**METHODS:** This prospective cross-sectional study (2012e2016) was performed at the 4 teaching hospitals in Addis Ababa, Ethiopia. All surgically treated TBI patients were included, and data on clinical presentation, injury types, and trauma causes were collected.

**RESULTS:** We included 1087 patients (mean age 29 years; 8.7% females; 17.1% <18 years old). Only 15.5% of TBIs were classified as severe (Glasgow Coma Scale score 3e8). Depressed skull fracture (44.9%) and epidural hematoma (39%) were the most frequent injuries. Very few patients had polytrauma (3.1%). Assault was the most common injury mechanism (69.9%) followed by road traffic accidents (15.8%) and falls (8.1%). More than 80% of patients came from within 200 km of the hospitals, but the median time to admission was 24 hours. Most assault victims (80.4%) were injured >50 km from the hospitals, whereas 46% of road traffic accident victims came from the urban area. Delayed admission was associated with higher Glasgow Coma Scale scores and nonsevere TBI (P < 0.01).

CONCLUSIONS: The injury panorama, delayed admission, and small number of operations performed for severe TBI are linked to a substantial patient selection bias both before and after hospital admission. Our results also suggest that there should be a geographical framework for tailored guidelines, preventive efforts, and development of prehospital and hospital services.

#### INTRODUCTION

ccording to recent global estimates, close to 90% of all trauma-related deaths occur in low- and middle-income countries (LMICs).<sup>1</sup> Neurological injuries are the most important causes of death and disability from trauma, particularly in children and young adults.<sup>2</sup> However, studies on head and spinal injuries from LMICs are underrepresented in the international literature.<sup>3,4</sup> Importantly, as different regions have their own needs and obstacles, neurotrauma research and

management must be contextualized. It is not feasible to directly transfer cost-demanding, evidence-based guidelines from Western countries to LMICs, which lack the necessary *fi*nances, equipment, and human resources. Thus, there is a great need for more and better data on epidemiologic aspects and the entire continuum of care to facilitate development of locally

# Key words

- Epidemiology
- Head injury
- Low- and middle-income countries
- Neurotrauma
- Traumatic brain injury

Abbreviations and Acronyms ASDH: Acute subdural hematoma CT: Computed tomography DSF: Depressed skull fracture ED: Emergency department EDH: Epidural hematoma GCS: Glasgow Coma Scale LMICs: Low- and middle-income countries OR: Odds ratio PBI: Penetrating brain injury RTA: Road traffic accident TBI: Traumatic brain injury

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tailored guidelines, improve quality of care, and identify region-specific focus areas for preventive efforts.<sup>5,6</sup>

Ethiopia is the second most populous country in Africa with about 115 million inhabitants.7 Notably, it is a country of young people, as 70% are <30 years of age.8 Ethiopia has one of the fastest growing economies in the world with a rapid rate of urbanization and industrialization and has some of the highest numbers of road traffic injuries and deaths worldwide.9,10 Fall accidents among construction workers are very common,<sup>10</sup> and there are high rates of injuries resulting from violence and assaults.<sup>11,12</sup> In studies from the emergency department (ED) at Black Lion Specialized Hospital in Addis Ababa, traumatic brain injury (TBI) was the leading cause of mortality and the most important indication for neurosurgical procedures.<sup>13-15</sup> The burden of trauma, especially neurotrauma, weighs heavily on Ethiopian society,11 and research that can lead to improved patient care and identify relevant focus areas for Ethiopian authorities is timely and highly warranted.

The Ethiopian/Norwegian training program in neurosurgery was started in 2006 and has been instrumental in developing a sustainable neurosurgical environment in Ethiopia.<sup>16</sup> A key issue for further development is research, particularly within the most prevalent disease conditions. To this end, we prospectively registered TBI patients who were surgically treated at the 4 teaching hospitals in Addis Ababa in the period 2012e2016. In this article, we describe the trauma causes, injury types, and clinical presentation. In another article, we report on the surgical treatment, complications, and patient outcomes.<sup>17</sup>

#### MATERIALS AND METHODS

#### Study Setting

This study was done at the 4 neurosurgical teaching hospitals in Addis Ababa, Ethiopia: Black Lion Specialized Hospital, Myung Sung Christian Medical Center, Alert Hospital, and Zewditu Memorial Hospital. These hospitals provide the majority of neurosurgical services in the country. Hospital management of TBI patients is based on the Advanced Trauma Life Support guidelines and the Brain Trauma Foundation guidelines.<sup>18</sup> More details on hospital management are described elsewhere.<sup>17</sup> This study is part of a larger collaborative research project approved by the Institutional Review Board, Addis Ababa University, Ethiopia, and by the Regional Ethical Committee, University of Bergen, Norway.

#### Patients and Data Collection

In this prospective cross-sectional study, we included all TBI patients who were surgically treated from October 2012 to December 2016. Most patients were treated at Black Lion Specialized Hospital and Myung Sung Christian Medical Center. Alert Hospital and Zewditu Memorial Hospital started treating TBI patients in 2015 but were not fully operational before 2016. Most patients treated at Alert Hospital and Zewditu Memorial Hospital were transferred from Black Lion Specialized Hospital or Myung Sung Christian Medical Center. Alert Hospital and Zewditu Memorial Hospital did not receive direct transfers from district hospitals.

Neurosurgical residents recorded data from admission until discharge using a paper-based case report form. The case report form included data on demographics; injury mechanism; time of injury; computed tomography (CT) *f*indings; extracranial injuries; surgical procedures; complications; survival; and dates of admission, surgical procedures, and discharge. The Glasgow Coma Scale (GCS) score was used to assess injury severity. TBIs were categorized as mild (GCS score 14e15), moderate (GCS score 9e 13), and severe (GCS score 3e8).

#### Statistical Analysis

Data were analyzed using IBM SPSS Version 21 software (IBM Corporation, Armonk, New York, USA). Clinical status was used as the dependent variable, and the effect of demographics, trauma mechanisms, geographical distance, and time interval between trauma and admission was investigated by binomial and multinomial regression analysis. Unless otherwise specified,  $C^2$  test was used to test for association between categorical variables, while *t* test and Mann-Whitney test were used for continuous variables. Missing data were checked for random distribution. A *P* value <0.05 was considered significant.

We analyzed predictors of severity categorized as severe (GCS score <9) or not severe using multivariate analysis. Main diagnosis (depressed skull fracture [DSF], epidural hematoma [EDH], acute subdural hematoma [ASDH], penetrating brain injury [PBI], traumatic intracerebral hematoma, miscellaneous), time to admission (cutoff 24 hours), trauma mechanism (assault, road traffic accident [RTA], fall, other), age (14e25, 26e35, 36e44, and >44 years), sex, and distance from trauma site to hospital (cutoff 200 km) were categorized, and logistic regression was used for analysis. Finally, we included the above-mentioned variables in a logistic regression model.

## RESULTS

#### Demographics and Injury Types

In the study period, 4412 TBI patients (90 patients from October to December 2012, 796 patients in 2013, 942 patients in 2014, 1284 patients in 2015, and 1300 patients in 2016) visited the ED of the 4 hospitals. A total of 1087 patients (24.6%) were surgically treated and included in this study. The mean age was 29 years, and 91.3% were males (Table 1). Female patients were younger than male patients (mean age 24.7 vs. 29.4 years; *P*<sub>4</sub> 0.01). Among all patients, 17.1% were children (<18 years old). The sex distribution was less skewed among children than adults (*P* < 0.01).

The most common injury type was DSF (44.9%), followed by EDH, ASDH, PBI, and traumatic intracerebral hematoma/contusion (Table 1). Among 1050 patients with registered TBI severity, 52.1% had mild injuries, 29.1% had moderate injuries, and 15.5% had severe injuries. Polytrauma was infrequent with only 34 cases. The most common concomitant injuries were long bone fractures (in 24 patients) and chest injuries (in 6 patients).

# Mechanism of Injury

The mechanism of injury was reported for 732 patients (Table 1). The most frequent cause of trauma was assault (69.9%) followed by RTAs (15.8%) and falls (8.1%). Supplemental Table 1 presents a detailed overview of injury mechanisms according to the *International Statistical Classification of Diseases and Related Health* 

Variable	Value
Number of patients	1087
Sex, male	992 (91.3%)
Age, years, mean SD	29.0 14.7
Patients <18 years old	186 (17.1%)
Head injury types	1087
DSF	488 (44.9%)
EDH	424 (39.0%)
ASDH	76 (7.0%)
PBI	74 (6.8%)
TICH/contusion	23 (2.1%)
Other	2 (0.2%)
Polytrauma	34 (3.1%)
Severity	1050
Mild	566 (52.1%)
Moderate	316 (29.1%)
Severe	168 (15.5%)
Injury mechanism	732
Assault	512 (69.9%)
RTA	116 (15.8%)
Fall	59 (8.1%)
Other	45 (6.1%)
Distance to hospital, km	1045
<200	854 (81.7%)
Time to admission, hours	705
Median (IQR)	24.0 (60)
Unless otherwise indicated, the provided values are counts with parentheses. DSF, depressed skull fracture; EDH, epidural hematoma; ASDH, acute si	th percentages in ubdural hematoma;

PBI, penetrating brain injury; TICH, traumatic intracerebral hematoma; RTA, road traffic accident; IQR, interquartile range.

Problems, Tenth Revision. Time to admission in hours was different for different injury mechanisms (Kruskal-Wallis test;  $C_3^2$  ¼ 44.7, P < 0.01), with a mean rank in time to presentation of 243.4 for RTAs, 372.6 for assault, 322.3 for falls, and 276.8 for other injuries (data not shown).

Assaults. There were 512 TBIs caused by assaults (Table 1). Assault was the most frequent cause of severe TBI (59%), but only 12.3% of 505 assault victims with documented TBI severity presented with a severe TBI (Table 2). The majority of assault victims (80.4%) came from outside of the city (Figure 1). Stick (50.4%) and thrown stone (21.6%) injuries were the most common types of assault (Supplemental Table 1). The most frequent injury types were DSF (45.3%), EDH (38.1%), and PBI (12.5%) (Table 3). Assault victims more often presented with a DSF or PBI than patients with other mechanisms of injury (Table 3). Gunshot injuries were transformed as severe TBIs (Supplemental Table 1).

*Road Traffic Accidents.* There were 116 cases of traffic-related TBIs (Table 1). Injury severity was documented in 112 patients, and 19.8% of these patients had a severe TBI (Table 2). Pedestrians accounted for 71.3% of cases (Supplemental Table 1). Victims of RTAs were frequently brought in from within 50 km of the hospitals (45.9%) (Figure 1) and were admitted earlier than other patients (P < 0.01) (Supplemental Table 1). EDH and DSF were the most frequent pathologies caused by RTAs (Table 3). EDH and ASDH were more common among RTA victims, whereas DSF was 65% less frequent in RTA victims compared with assault victims (Table 4).

*Falls*. A severe TBI occurred in 23.7% of 59 fall accidents (Tables 1 and 2). Falls from ladders, buildings, stairs, or scaffolding accounted for 42.4% of cases (Supplemental Table 1). EDH and DSF were the most common (86.4%) injuries caused by falls (Table 3).

Miscellaneous. Other trauma mechanisms were encountered in 45 cases (Table 1). Injury severity was documented in 44 cases, of which 15.9% were severe (Table 2). Most of these injuries were related to animals, caused by falling objects, or related to sport activities (Supplemental Table 1). Severe TBIs were typically seen in elderly farmers who were gored, kicked, or stamped on by their cattle. DSF and EDH were the most frequent (80%) injury types (Table 3).

# Distance from Hospital and Time to Admission

Distance from the accident scene to the hospitals was recorded for 1045 patients (Table 1). Most patients (81.7%) were injured <200 km from the hospitals (i.e., they came from Addis Ababa or neighboring areas) (Table 1 and Figure 1).

Table 2. Head Injury Severity and Mechanism of Injury for 720 Patients				
	RTA	Assault	Fall	Other
Severe	22 (21.0%)	62 (59.0%)	14 (13.3%)	7 (6.7%)
Moderate	32 (15.5%)	148 (71.5%)	12 (5.8%)	15 (7.2%)
Mild	58 (14.2%)	295 (72.3%)	33 (8.1%)	22 (5.4%)

The provided values are counts with percentages in parentheses. Head injury severity is defined as severe (GCS score 3e8), moderate (GCS score 9e13), and mild (GCS score 14e15). RTA, road traffic accident; GCS, Glasgow Coma Scale.

Time from injury to admission was registered for 705 patients (Table 1). The median time from injury to admission was 24 hours, and time to admission was strongly related to the distance from the hospitals (P < 0.01). There was a statistically significant difference in admission GCS score between the different categories of time to admission (P < 0.01) (Table 5). Patients who presented within 6 hours of injury had the lowest mean GCS score (11.22), and patients who presented >120 hours after injury had the highest GCS score (14.04).

#### Predictors of Severity

In bivariate analysis, we found a lower risk of severe TBI with DSF (P < 0.01) or assault (**P**<sub>4</sub> 0.04) compared with other diagnoses or injury mechanisms. Patients with long transportation times were also less likely to present with a severe TBI (P < 0.01). Sex, distance from hospital, and age were not significantly associated with severity.

Using DSF and assault as references for diagnosis and mechanism, respectively, we included the above-mentioned variables into a logistic regression model to analyze predictors of severe TBI (Table 6). EDH (odds ratio [OR]¼3.5), ASDH (OR¼6.3), and falls (OR ¼ 2.8) were significant predictors of a severe injury. A long transportation time was significantly associated with nonsevere injuries (OR ¼ 0.3).

#### DISCUSSION

In this study, we present novel data on TBI patients who were surgically treated in Ethiopia. Most patients were male adolescents or young adults with a mean age <30 years. DSF and EDH were the most frequent (>80%) injury types, and the majority of patients (>50%) had a GCS score of 14e15 at presentation.

Approximately 70% of TBI patients were injured in assaults. Hospital admission was often delayed with a median time to admission of 24 hours. Delayed admission was associated with a nonsevere TBI and vice versa.

Most patients in our study came from outside of Addis Ababa, and we found a longer time to admission than reported in other studies.<sup>4,12,19</sup> Long transportation times were significantly associated with better GCS scores. Importantly, there are usually no prehospital services, and patients are typically taken to the hospital in private cars or taxis.<sup>20</sup> Ambulance transports are usually reserved for interhospital transfers because of lack of neurosurgical services or CT scanners at district hospitals, and ambulances are usually not staffed with paramedics.<sup>3</sup> Thus, there is a selection bias where severely injured patients at distant sites die before reaching the neurosurgical center, at the site, during transport, or at district hospitals. This is clearly indicated by the positive correlation between injury severity (i.e., GCS score) and time to admission as well as the low numbers of ASDH, PBI, and traumatic intracerebral hematoma/contusion, usually associated with a higher injury severity. Moreover, there is also a selection bias at the neurosurgical centers where patients in poor condition are not operated on. Intensive care unit admission and surgical treatment are usually prioritized for patients with a GCS score of  $5 \ge$  and normal pupillary responses, as it is believed that these patients have a better



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Table 3. Main Diagnosis and Injury Mechanism for 732 Patients						
	RTA	Assault	Fall	Other		
DSF	33 (10.6%)	232 (74.6%)	25 (8.0%)	21 (6.8%)		
EDH	65 (21.6%)	195 (64.8%)	26 (8.6%)	15 (5.0%)		
ASDH	14 (32.6%)	16 (37.2%)	6 (14.0%)	7 (16.3%)		
PBI	1 (1.5%)	64 (97.0%)	0 (0.0%)	1 (1.5%)		
TICH/contusion	2 (20.0%)	5 (50.0%)	2 (20.0%)	1 (10.0%)		
Other	1 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		
The provided values are counts with percentages in parentheses. RTA. road traffic accident: DSF. depressed skull fracture: EDH. epidural hematoma: ASDH. acute subdural hematoma: PBI. penetrating brain iniury: TICH. traumatic intracerebral hematoma.						

prognosis. Notably, a study from Black Lion Specialized Hospital in Addis Ababa showed 50.8% mortality of severe TBI in the ED, and 62% of the survivors were operated on.<sup>3</sup>

The predominance of male patients and young patients as well as the infrequency of injured children has been reported previously.<sup>21-25</sup> The high proportion of assaults is distinctive from many studies in both developed and developing countries,<sup>26,27</sup> but reflects a selection bias of less injured patients for surgery. TBI not associated with RTAs, such as TBI associated with assault, was also found to be significantly associated with receiving surgery in recent studies from referral hospitals in Uganda<sup>28</sup> and Tanzania.<sup>29</sup> Most of the registered assaults in our study occurred in rural areas outside of Addis Ababa; interestingly, this has also been noted in other reports comparing rural and urban areas.<sup>23,30</sup> Stick injuries were the most frequent type of assault. Notably, close to 80% of the Ethiopian population live in rural areas, and it is very common in these areas to carry sticks for selfdefense and for support during long hours of work and commuting.<sup>31</sup> Interestingly, stick injuries are frequently seen on the left side of the head, as most people are right-handed. Sticks cause a focal low-energy trauma to the head, which is less likely to result in severe depression of consciousness.<sup>32</sup> Assault victims therefore typically present with a high GCS score and CT findings of DSF and/or EDH. In a comparable study, Peeters et al.<sup>33</sup> reported similar findings of frequent DSFs.

Motorization and urbanization are rapidly developing in the sub-Saharan region, and RTAs are increasing.<sup>4,21,26</sup> In our study, RTAs were the second most frequent cause of TBI. As previously reported from LMICs,<sup>6,22,34</sup> we found that most RTAs involved pedestrians. Pedestrians were also brought in earlier than vehicle occupants, usually in the offending vehicle, whereas car occupants have to wait for transportation. As opposed to assaults, patients admitted after RTAs were more frequently from urban areas. This indicates a geographical distribution of vehicle density, but also a selection bias of less severe injuries, as discussed above.

Table 4. Logis	tic Regression Analysis of Inju	ry Type and Injury Mechanism				
Туре	Mechanism	Yes, number (%)	No, number (%)	OR (95% CI)		
DSF	Assault	293 (57.2%)	219 (42.8%)	1.00		
	RTA	37 (31.9%)	79 (68.1%)	0.35 (0.23,0.54)		
	Fall	27 (45.8%)	32 (54.7%)	0.63 (0.37,1.10)		
	Other	25 (55.6%)	20 (44.4%)	0.93 (0.51,1.72)		
ASDH	Assault	18 (3.5%)	494 (96.5%)	1.00		
	RTA	15 (12.9%)	101 (87.1%)	4.1 (2.0, 8.4)		
	Fall	6 (10.2%)	53 (89.8%)	3.1 (1.2, 8.2)		
	Other	7 (15.6%)	38 (84.4%)	5.1 (2.0, 12.9)		
EDH	Assault	203 (39.6%)	309 (60.4%)	1.00		
	RTA	64 (55.2%)	52 (44.8%)	1.9 (1.25, 2.81)		
	Fall	26 (44.1%)	33 (55.9%)	1.2 (0.70, 2.10)		
	Other	16 (35.6%)	29 (64.4%)	0.84 (0.45, 1.60)		
OR. odds ratio: Cl. o	OR odds ratio: CL confidence interval: DSF. Devrased skull fracture: RTA road traffic accident: ASDH acute subdural hematoma: FDH enidural hematoma					

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Table 5. Glasgow Coma Scale Scores for 693 Patients with Categorized Time to Admission						
Time to Admission (hours)	GCS Score (mean SD)	Number of Patients				
<6	11.22 3.7	85				
6e12	11.05 3.9	74				
12e24	11.67 3.7	189				
24e72	12.77 3.0	175				
72e120	13.05 2.7	87				
>120	14.04 2.1	83				
GCS, Glasgow Coma Scale.						

Fall accidents were the third most common cause of TBI. The number of fall accidents would probably have been higher if we included patients who died at the scene of the accident and patients who received nonsurgical treatment. Work-related falls were most frequent in our study and are associated with many large-scale construction projects in the city and poor precautionary measures. This contrasts with the changing epidemiologic panorama of high-income countries, where there is an increasing incidence of fall-related TBIs among elderly adults.<sup>34</sup>

In our study, 1087 (24.6%) patients were operated on for a TBI over a 4-year period out of 4412 TBI patients who presented to the ED of our 4 hospitals. Only 2 hospitals in Addis Ababa were operational the entire study period, and there was approximately 1 neurosurgeon per 4 million inhabitants.<sup>16</sup> Surgical activity is increasing year by year, and >2000 neurosurgical procedures are now performed every year. In a recent study from the main tertiary hospital in Uganda looking at all admitted TBI patients in the period 2014e2015, only 242 (19%) of 1247 patients were operated on.<sup>28</sup> In a similar study from a referral hospital in

Table 6. Multivariate Regression Analysis of Predictors of Injury Severity							
	df	P Value	OR	95% CI			
Diagnosis							
DSF (reference)							
EDH	1	0.000	13.5	4.951, 28.346			
ASDH	1	0.000	26.3	6.421, 52.258			
PBI	1	0.001	6.7	1.967, 19.293			
TICH	1	0.002	21.5	2.718, 135.504			
Injury mechanism							
Assault (reference)							
RTA	1	0.972	1.0	0.53, 1.93			
Fall	1	0.012	2.8	1.25, 6.24			
Other	1	0.655	0.8	0.27, 2.3			
>24 hours	1	0.000	0.344	0.203, 0.584			
>200 km	1	0.25	0.68	0.355, 1.307			
Age groups							
18e44 years (reference)							
45e65 years	1	0.78	1.15	0.43, 3.05			
>65 years	1	0.25	1.9	0.64, 5.55			
0e17 years	1	0.38	0.35	0.034, 3.64			
OR, odds ratio; CI, confidence interval; DSF, depressed skull fracture; EDH, epidural hematoma; ASDH, acute subdural hematoma; PBI, penetratine brain iniury: TICH. traumatic intracerebral							

OR, odds ratio; CI, confidence interval; DSF, depressed skull fracture; EDH, epidural hematoma; ASDH, acute subdural hematoma; PBI, penetrating brain injury; TICH, traumatic intracerebral hematoma; RTA, road traffic accident.

Tanzania of 2502 TBI patients admitted in the period 2013e2017, only 609 (24%) received surgery.<sup>29</sup> Taken together, although relatively few patients underwent surgery, the latter study showed a variable but clear benefit of surgery for all TBI severities, providing a clear rationale for further development of neurosurgical services in sub-Saharan Africa.

#### CONCLUSIONS

TBI is a major public health problem in Ethiopia, and our novel data on neurosurgical management of TBI can help to improve the quality of care and identify focus areas for preventive efforts. Many young patients die or experience significant treatment delay because of limitations within prehospital services and local hospitals, and efforts should be made to address this (e.g., trauma resource allocation, ambulance services, systematic referral systems from district hospitals, telemedicine programs, increased CT accessibility, neurosurgical education and outreach programs).<sup>35-37</sup> Furthermore, as more patients survive acute TBI surgery, rehabilitation should become a more integral part of treatment.

Many of these issues are not unique to the neurosurgical domain and can be addressed by more resources or better use of

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the resources at hand. Moving ahead, prioritizations and solutions should be discussed between local and national governmental officials, health care leaders, and medical experts. Public awareness campaigns, safety standards, and legislative measures could further help to reduce the detrimental consequences of TBI in Ethiopia. Specifically, there should be prevention strategies against stick injuries, such as consideration of a ban of the use of sticks in public places or awareness campaigns about the detrimental consequences of stick injuries.

# CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Tsegazeab Laeke: Methodology, Formal analysis, Writing - original draft, Writing - review & editing. Abenezer Tirsit: Methodology. Azarias Kassahun: Methodology. Abat Sahlu: Investigation. Tequam Debebe: Investigation. Betelehem Yesehak: Investigation. Samuel Masresha: Investigation. Negussie Deyassa: Formal analysis. Bente E. Moen: Writing - original draft. Morten Lund-Johansen: Methodology, Formal analysis, Writing - original draft. Terje Sundstrøm: Methodology, Formal analysis, Writing - origiinal draft, Writing - review & editing.

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# SUPPLEMENTARY DATA

Injury Mechanism	Number of Patients	Time to Admission (hours)y	Age (years)z
Assault	504	48.0 (78)	29.5 11.7
Stick injury (Y00)	254 (50.4%)		
Hit by a sharp object (X99)	89 (17.7%)		
Hit by a thrown stone (W20)	109 (21.6%)		
Punched	1 (0.2%)		
Assault by hanging, strangulation and suffocation (X91)	8 (1.6%)		
Assault by rifle or shotgun (X94)	42 (8.3%)		
Blast injury (X96)	1 (0.2%)		
Road traffic accident	115	12.0 (43)	28.7 15.6
Pedestrian run over by 2/3-wheeled vehicle (V02)	10 (8.7%)		
Pedestrian run over by a car (V03)	72 (62.6%)		
Occupant of 3-wheeled motor vehicle injured in transport accident (V30-V39)	5 (4.3%)		
Car occupant injured in transport accident (V40-V49)	22 (19.1%)		
Injured riding a motorcycle (V20-V29)	6 (5.2%)		
Fall	59	24.0 (84)	29.4 20.3
Fall from stairs (W10)	4 (6.8%)		
Fall from ladder (W11)	1 (1.7%)		
Fall from, out of, or through building or structure (W13)	11 (18.6%)		
Fall from scaffolding (W12)	9 (15.3%)		
Fall from tree (W14)	12 (20.3%)		
Fall from cliff (W15)	7 (11.9%)		
Fall from standing position (W01)	11 (18.6%)		
Fall pediatrics	3 (5.1%)		
Fall from stationary car (V58.2)	1 (1.7%)		
Animal-related injuries	22	24.0 (39)	39.3 21.7
Horse kick	9 (40.9%)		
Attacked by cattle	2 (9.1%)		
Fall from horse	11 (50%)		
Sports injury	1		
Trivial trauma	5		
Hit by falling object	17		
Unknown mechanism	31		
*https://icd.who.int/Drowse10/2016/en#/V20-V29. yMedian (interquartile range). zMean SD.			

# Paper II

# Prospective Study of Surgery for Traumatic Brain Injury in Addis Ababa, Ethiopia: Surgical Procedures, Complications, and Postoperative Outcomes

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BACKGROUND: Traumatic brain injury (TBI) is an important cause of trauma-related mortality and morbidity in Ethiopia. There are significant resource limitations along the entire continuum of care, and little is known about the neurosurgical activity and patient outcomes.

■ METHODS: All surgically treated TBI patients at the 4 teaching hospitals in Addis Ababa, Ethiopia were prospectively registered from October 2012 to December 2016. Data registration included surgical procedures, complications, reoperations, discharge outcomes, and mortality.

RESULTS: A total of 1087 patients were included. The most common procedures were elevation of depressed skull fractures (49.5%) and craniotomies (47.9%). Epidural hematoma was the most frequent indication for a craniotomy (74.7%). Most (77.7%) patients were operated within 24 hours of admission. The median hospital stay for depressed skull fracture operations or craniotomies was 4 days. Decompressive craniectomy was only done in 10 patients. Postoperative complications were seen in 17% of patients, and only 3% were reoperated. Cerebrospinal fluid leak was the most common complication (7.9%). The overall mortality was 8.2%. Diagnosis, admission Glasgow Coma Scale (GCS) score, surgical procedure, and complications were significant predictors of discharge GCS score

#### Key words

- Low- and middle-income countries
- Neurotrauma
- Surgical outcome
- Traumatic brain injury

# Abbreviations and Acronyms

ASDH: Acute subdural hematoma CSF: Cerebrospinal fluid CT: Computed tomography DC: Decompressive craniectomy DSF: Depressed skull fracture ED: Emergency department EDH: Epidural hematoma GCS: Glasgow Coma Scale HIC: High-income country ICU: Intensive care unit HIC: Low- and middle-income country (P < 0.01). Age, admission GCS score, and length of hospital stay were significantly associated with mortality ( $P \pm 0.005$ ).

CONCLUSIONS: The injury panorama, surgical activity, and outcome are significantly influenced by patient selection due to deficits within both prehospital and hospital care. Still, the neurosurgical services benefit a large number of patients in the greater Addis region and are qualitatively comparable with reports from high-income countries.

# INTRODUCTION

he majority of trauma-related mortality worldwide occurs in low- and middle-income countries (LMICs), and traumatic brain injury (TBI) is the leading cause of death.<sup>1</sup> The estimated TBI incidence in sub-Saharan Africa is 801 per 100,000, and the mortality rate for severe TBI is approximately 50%.<sup>2,3</sup> TBI is particularly frequent in younger people,<sup>4</sup> and Ethiopia has more than 70 million citizens younger than 30 years of age.<sup>5,6</sup> TBIrelated injuries and deaths therefore take a significant toll on society.<sup>7,8</sup> In a recent Ethiopian study of 4206 postmortem reports, 67% of deaths were caused by accidents, homicide, and suicide.<sup>9</sup>

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OR: Operating room PBI: penetrating brain injury TBI: Traumatic brain injury

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Almost 40% of deaths were accidental, of which close to 70% were traffic related. Moreover, in a study from an Ethiopian emergency department (ED) of almost 10,000 patients, TBI was the most common cause of mortality, causing close to 23% of all deaths.<sup>10</sup>Many TBI patients in sub-Saharan Africa do not have adequate access to neurosurgical treatment,<sup>11</sup> and there are substantialdeficits throughout the entire chain of care.2,12,13 Prehospitalcare is underdeveloped, and ambulance personnel usually lackappropriate training.<sup>2,12</sup> Few neurosurgeons and centers that canprovide neurosurgical treatment.<sup>14,15</sup> Those that exist have significant shortages when it comes to equipment. infrastructure, and human resources in the ED, operating rooms (OR), intensive care units (ICU), and wards. Guidelines for the management of severe TBI are also missing or poorly adapted.<sup>16</sup> Many patients who survive the initial phase end up in health centers or hospitals that are even less capable of giving proper or timely treatment.<sup>2,12</sup> Rehabilitation is virtually nonexistent, and most TBI survivors are left to be cared for by their families. These limitations result in a substantial selection of patients, where many succumb to their injuries before reaching definitive care and many are not operated on because their prognosis is considered poor. However, it is largely unknown how these limitations affect the complication rate and outcome of those who are operated on as structured registries capturing data on the clinical care and outcome of patients are lacking.<sup>17</sup> This knowledge can potentially help to develop tailored guidelines, improve patient care, and identify focus areas for preventive efforts.4,18,19

Building on the Ethiopian/Norwegian training program in neurosurgery,<sup>20</sup> we established a prospective TBI database at the 4 teaching hospitals in Addis Ababa. Here, we present the surgical procedures, postoperative complications, and discharge outcomes for surgically treated TBI in the period 2012e2016. Predictors of postoperative complications and mortality were also identified. Trauma causes, injury types, and clinical presentation are described elsewhere.<sup>21</sup>

#### MATERIAL AND METHODS

#### Study Setting

This study was done at Black Lion Specialized Hospital, Myung Sung Christian Medical Center, Zewditu Memorial Hospital, and Alert Hospital in Addis Ababa, Ethiopia. These 4 neurosurgical teaching hospitals are currently the main providers of neurosurgical care in the country. Most TBI patients in this study were treated at Black Lion Specialized Hospital and Myung Sung Christian Medical Center. Zewditu Memorial Hospital and Alert Hospital *fi*rst started treating TBI patients in 2015 and were not fully operational before 2016. Regulatory approvals were obtained from the Institutional Review Board (003/16/surg), Addis Ababa University, Ethiopia, and by the Regional Ethical Committee (2018/53), University of Bergen, Norway.

#### Study Design and Data Collection

This was a prospective cohort study on surgically treated TBI patients. Data were prospectively collected from October 2012 to December 2016, and all surgically treated TBI patients were registered by neurosurgical residents using a paper-based case report form. The case report form included demographic information, cause of trauma, time of injury, computed tomography (CT) findings, other injuries, surgical procedures, postoperative complications, mortality, and time of events. The Glasgow Coma Scale (GCS) score was registered at admission and discharge. TBIs were defined as mild (GCS score 14e15), moderate (GCS score 9e 13), and severe (GCS score 3e8).<sup>22</sup>

#### **Statistical Analysis**

Data were analyzed using SPSS version 21 (SPSS Inc., Chicago, Illinois, USA). Age, time to admission, geographic distance, clinical status at admission, and diagnosis were used as independent variables. Discharge clinical status, presence of postoperative complications, duration of hospital stay, and mortality were used as dependent variables. Binomial and multinomial regression analyses were used to assess how much the independent variables affected the dependent variables. Chi-square test was used for categorical variables. The Student's t-test and Mann-Whitney U test were used for continuous variables. Missing data were checked for random distribution. A P value <0.05 was considered significant.

#### EMERGENCY CARE OF TRAUMATIC BRAIN INJURY PATIENTS

Prehospital services are not well developed in Ethiopia, and ambulances are not equipped with trained paramedics.<sup>2</sup> As a consequence, families or bystanders usually bring patients to the hospitals. Ambulances are typically used for interhospital transfers, and nurses often escort severe TBI patients during such transports. During the study period, Zewditu Memorial Hospital and Alert Hospital did not receive direct transfers from district hospitals. Most patients treated at these 2 hospitals were transferred from either Black Lion Specialized Hospital or Myung Sung Christian Medical Center.

At admission, TBI patients were *fi*rst evaluated by intern physicians in the ED. Emergency medicine physicians were also available in the ED. After registration of vital signs and clinical suspicion of a TBI, responsibility was transferred to neurosurgery residents supported by an on-call consultant neurosurgeon. Emergency TBI management was based on the Advanced Trauma Life Support guidelines and Brain Trauma Foundation guidelines.<sup>23,24</sup>

A head CT was generally done for all patients with moderate and severe TBI. The Canadian CT head rule was followed for patients with mild TBI.<sup>25</sup> CT scanning services and radiology expertise was available 24-7 at Black Lion Specialized Hospital and Myung Sung Christian Medical Center. Zewditu Memorial Hospital and Alert Hospital did not have CT scanners, and patients transferred to these centers brought CT scans from other centers.

#### Standards of Perioperative Care

Surgical protocols were similar at the 4 neurosurgical teaching hospitals. Salvageable patients were given priority for surgical treatment, and patients with an admission GCS score of 3e4 and/ or *fixed* and dilated pupils were generally not intubated, treated in the ICU, or operated.<sup>26</sup> Families of these patients were counseled thoroughly about the fatal prognosis. There were 6 ICU beds and 4

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mechanical ventilators at Black Lion Specialized Hospital during the study period, and these resources were shared with other surgical departments. Myung Sung Christian Medical Center was equipped with 8 ICU beds and 8 mechanical ventilators, and these resources were shared with other surgical and medical departments. Zewditu Memorial Hospital and Alert Hospital had operative ICUs from 2016 with 3 ICU beds and 1 mechanical ventilators, respectively.

Patients with severe TBI were intubated and sedated in the ED by emergency medicine physicians. For other patients, this was done in the OR. Preparation and draping of the surgical site were done by the operating surgeons, a senior resident with 4e5 years of training and a junior resident. In a few cases, a consultant attended the procedures. All patients received prophylactic antibiotics (typically ceftriaxone) just before induction of anesthesia, and this was continued postoperatively for 24 hours. Patients with open fractures or contaminated wounds were started on antibiotics in the ED. One suction device plus monopolar and bipolar cautery were available. Hemostatic agents (e.g., Surgicel) were occasionally available via visiting neurosurgeons. Duraplasties were performed using pericranial tissue or fascia lata (glue or dura substitutes were not available). For craniotomies, blood was routinely cross-matched and prepared. Patients were transfused if they bled more than the allowable blood loss. This was calculated by multiplying the estimated blood volume of the patient with by the difference between the patient's hematocrit and target hematocrit and dividing it by the patient's hematocrit.

Depressed skull fractures (DSFs) were treated if they were compounded or closed with significant depression and associated neurologic deficit.<sup>27</sup> A compound DSF was treated primarily with debridement and elevation.<sup>27,28</sup> If the wound edges were contaminated, thorough irrigation and debridement would be done. The wound would then be extended to expose all the edges of the depressed bone fragment. A burr hole would be done adjacent to the depressed bone edge, and the fractured bone segment would circumferentially be freed and removed.<sup>29</sup> Dural tears were closed using sutures and/or fascia, and watertightness was checked with Valsalva maneuver. If there was no infection associated with the wound, the removed bone would be generously washed and replaced.

Craniotomies were done using a Hudson drill and Gigli saw and typically lasted 2 hours or more. Epidural hematomas (EDHs) were treated according to the Brain Trauma Foundation guidelines.<sup>23</sup> A large trauma craniotomy (minimum 12 cm) was routinely done for all patients with an acute subdural hematoma (ASDH).<sup>30</sup> The decision to do a decompressive craniectomy (DC) adhered to published consensus statements.<sup>30</sup> An expansile duraplasty was performed if there was established or anticipated brain edema. It was customary to close with a floating bone flap if there was no brain edema above the inner table of the skull. If it was difficult to replace the bone, a DC would be done and the bone flap would be stored subcutaneously in the abdomen and typically replaced 3 months later.

Patients with severe TBI were routinely transferred intubated to the ICU after surgery. They were transferred to the ward when they showed improvement in their neurologic status. Neurologic development (vital signs, GCS score, pupillary reactions, motor function, and occurrence of seizures) was monitored and documented on a neurologic observation chart. Intracranial pressure monitors were not available. The ICU was equipped with mechanical ventilators and standard monitors and managed by 1 anesthesia resident with a daily morning round with a senior anesthesiologist. There was 1 nurse per 2 ICU patients. A postoperative CT scan was not done routinely unless patients displayed significant neurologic deterioration.

Other patients were transferred from the OR to the ward a few hours after extubation. Resources were limited at the ward, but some routines were present (e.g., urethral catheterization, transnasal oxygen, administration of drugs, insertion of nasogastric tubes and wound care). However, most of the care, mobilization and physical rehabilitation were done by relatives who were instructed by a nurse or physiotherapist. Patients were discharged when there was marked improvement in their clinical condition and after relatives were thought to be able to care for the patient.

## RESULTS

#### Surgical Procedures and Length of Hospital Stay

Trauma causes, injury types, and clinical presentation of our patient population were reported elsewhere.<sup>21</sup> In short, the most common trauma cause and injury type were assault and DSF, respectively. A total of 1087 TBI patients were operated, mean age was 29 years, 91.3% were males, 17.1% were <18 years, 15.5% of TBIs were severe, and 3.1% had polytrauma.

The most frequent diagnoses were DSF (44.9%) and epidural hematoma (EDH) (39%), and the most common surgical procedures were elevation of a DSF (49.5%) and craniotomy (47.9%; Table 1). A craniotomy was most often done for an EDH (74.7%) and ASDH (12.7%; Table 2).

Most (77.7%) patients were operated within 24 hours of admission, 13.7% patients were operated the next day, and the remaining (8.6%) were operated after 2 days or more. The majority of patients with a severe TBI (88.7%) were operated within 24 hours of admission; corresponding figures for moderate and mild TBI were 87% and 69.3%, respectively (P < 0.01).

The median length of hospital stay for a craniotomy or elevation of a DSF was 4 days while patients undergoing a DC stayed a median of 9 days. However, only 10 patients underwent a DC. There was a significant difference in the length of hospital stay between different diagnoses (P < 0.01; see Table 1).

#### Complications

Postoperative complications were seen in 17% of patients and 3% were reoperated (Table 3). The most common complication was cerebrospinal fluid (CSF) leak, which was seen in 7.9% of patients. Wound infection and hematomas were seen in 3.6% and 1.2% of patients, respectively. Wound infection was the most common cause of reoperation (39.4%). The complication rates for craniotomy and elevation of DSF were 21% and 12.8%, respectively. Patients with a wound infection had the longest hospital stays (median 21 days; data not shown). GCS score was the only significant predictor of postoperative complications in a logistic regression model including GCS score, age, time to admission, and surgical procedure (Table 4).

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	Number (%)	Median Length of Stay, IQR (days)
Injuries	1087	
Depressed skull fracture	488 (44.9)	4 (4)
Epidural hematoma	424 (39.0)	4 (4)
Acute subdural hematoma	76 (7.0)	5 (12)
Penetrating brain injury	74 (6.8)	7 (12)
Traumatic intracerebral hemorrhage/ contusion	23 (2.1)	11 (13)
Other	2 (0.2)	12
Procedures	1087	
Craniotomy	521 (47.9)	4 (6)
Elevation of depressed skull fracture	538 (49.5)	4 (3)
Decompressive craniectomy	10 (0.9)	9 (28)
Burr hole	13 (1.2)	3 (7)
Other	5 (0.5)	61
Severity	1050	
Mild (GCS score 14e15)	566 (52.1)	4 (3)
Moderate (GCS score 9e13)	316 (29.1)	5 (5)
Severe (GCS score <9)	168 (15.5)	8 (14)
Time to surgery	705	
Hours, median (IQR)	24.0 (60)	
Length of stay is the time from admission to disch	arge.	

IQR, interquartile range; GCS, Glasgow Coma Scale.

Most patients (75.3%) lost <500 mL of blood while 13.3% lost 500e1000 mL. Blood transfusion was most commonly needed for DC (40%). Only 5.6% of craniotomy patients and 0.4% of patients undergoing elevation of a DSF required transfusion.

Procedure and blood transfusion were strongly associated (P < 0.01).

Table 3. Postoperative Complications and Reoperations					
Surgical Procedure	Complications (N [ 185)	Reoperations (N [ 33)			
Craniotomy	109	16			
Hematoma	13	5			
CSF leak	44	4			
Pneumonia	28				
Wound infection	20	4			
Other	4	3			
Elevation	69	14			
Hematoma		2			
CSF leak	40				
Pneumonia	8				
Wound infection	17	8			
Other	4	4			
Burr hole	2				
CSF leak	2				
Decompressive craniectomy	3	1			
Pneumonia	1				
Wound infection	1				
Other	1	1			
Other	2	2			
Wound infection	1	1			
Other	1	1			
CSF, cerebrospinal fluid.					

#### Mortality

The overall mortality in our operated patients was 8.2%. Among 78 patients with recorded dates of admission and death, 15 died within 24 hours, 37 within a week, and the remaining 26 after more than a week.

Postoperative complications were seen in 46.1% of the patients who died. The odds of dying were higher in those who had

Table 2. Surgical Procedures and Main Diagnosis							
Surgical Procedure	DSF	EDH	ASDH	PBI	tICH	Other	Total
Elevation of DSF	481 (89.4)	21 (3.9)	3 (0.6)	33 (6.1)			538
Craniotomy	7 (1.3)	389 (74.7)	66 (12.7)	40 (7.7)	17 (3.3)	2 (0.4)	521
Burr hole		12 (92.3)			1 (7.7)		13
DC		2 (20.0)	7 (70.0)	1 (10.0)			10
Other					5 (100)		5

DSF, depressed skull fracture; EDH, epidural hematoma; ASDH, acute subdural hematoma; PBI, penetrating brain injury; tICH, traumatic intracerebral hematoma/contusion; DC, decompressive craniectomy.

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					95% EXP	CI for (B)
	В	SE	Sig.	Exp (B)	Lower	Upper
Age (years)	0.001	0.007	0.839	1.001	0.987	1.016
Admission GCS score	0.165	0.029	0.000	1.179	1.114	1.248
Time from injury to admission (hours)	-0.001	0.000	0.209	0.999	0.998 1	.000
Decompressive craniectomy (yes/ no)	—0.493	1.240	0.769	0.773	0.054 6.	.949
Craniotomy (yes/no)	-0.257	0.876	0.769	0.773	0.139	4.307
Elevation of DSF (yes/no)	-0.299	0.875	0.732	0.741	0.133	4.120
Postoperative complications are catego SE, standard of error; CI, confidence in	orized as nterval; D	present SF, dep	(yes) or ressed s	r absent kull frac	(no). ture.	

postoperative complications as compared with those who had an uneventful course (odds ratio  $\gamma_4$  4.908; 95% CI, 3.11e7.7; P < 0.01). Moreover, the mean discharge GCS score was lower in patients with complications than in those without complications (GCS score 10.6 vs. 12.6; P < 0.01). The amount of blood loss and mortality were significantly associated (P < 0.01); 32.3% of those who lost >1000 mL of blood died.

We compared time to admission, age, and diagnosis among survivors and fatalities (Table 5). For patients who died, the mean rank of time from accident to admission was shorter and the mean age was higher (P < 0.01). The highest and lowest mortality rates were found in ASDH and DSF, respectively (P < 0.01).

Admission GCS score was strongly associated with mortality (P < 0.01; Figure 1). Among 168 patients with severe TBI, there were 42.3% deaths. A severe TBI with ASDH was associated with a

	Fatalities	Survivors	Total	P Value
Mean rank of time to admission (hours)	227.95	362.55		<0.01
Mean age (years)	35.8	28.3		<0.01
Diagnoses (n %)				<0.01
Depressed skull fracture	7 (1.5)	481 (98.5)	488	
Epidural hematoma	41 (9.7)	383 (90.3)	424	
Acute subdural hematoma	30 (39.4)	46 (60.5)	76	
Penetrating brain injury	8 (10.8)	66 (89.2)	74	
Total	86	976	1062	



mortality rate of 54.1% while the corresponding rates for moderate and mild TBI with ASDH were 25% and 10%, respectively (P < 0.01; Table 6). Comparable figures for EDH were 36.7% (severe TBI), 2.7% (moderate TBI), and 0.6% (mild TBI; P < 0.01).

Univariate analysis showed ASDH patients to be  $45\times$  more likely to die than DSF patients. After adjusting for age, injury mechanism, and time to admission, the odds of dying from an ASDH was approximately 34.5 (Table 6). Patients with EDH had about 7.7×higher risk of dying. Furthermore, we did a regression analysis including age, GCS score, time to admission, and length of stay. We found age, GCS score, and length of stay to be significantly associated with mortality (Table 7). Diagnosis and surgical procedure had a collinear relationship, but this was not significant in multivariate analysis.

#### **Discharge Outcome**

At discharge, 856 out of 1036 eligible patients had GCS score 14e 15 (mild TBI), 87 had GCS score 9e13 (moderate TBI), 4 had GCS score 3e8 (severe TBI), and 89 were dead. Age, diagnosis, admission TBI severity, surgical procedure, and complications were investigated as possible predictors in patients with discharge GCS score 9e15 (three cases with GCS score 3 and deaths were excluded). Age was not significant, whereas diagnosis, admission GCS score, procedure, and complications were all significant predictors of discharge GCS score (P < 0.01).

#### DISCUSSION

In this study, we present novel data on surgical procedures and outcome of TBI patients in Ethiopia. The most common surgical procedures were elevation of a DSF and craniotomy for EDH. Significant delays along the entire continuum of care were associated with a substantial patient selection both before and after admission to neurosurgical centers.<sup>21</sup> This has important consequences for the injury panorama, surgical activity, and patient outcome. Procedures like elevation of a DSF and craniotomy for EDH are therefore significantly overrepresented in our study as compared with implantation of intracranial

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Mortality Risk, Fatalities Survivors Adjusted Number (%) Number (%) Total OR (95% CI) P Value DSF 7 481 14 1 6 (42.9) 106 Severe 8 (57.1) Moderate 1 (0.9) 105 (99.1) 351 Mild 0 351 (100) 17 ٥ 17 Missing 14 ASDH 30 46 76 34.51 (8.78, 135.60) 0.000 Severe 20 (54.1) 17 (45.9) 37 Moderate 6 (25.0) 18 (75.0) 24 Mild 1 (10.0) 9 (90.0) 10 2 5 Missing 3 41 EDH 383 424 7.73 (2.26, 26.4) 0.001 Severe 36 (36.7) 62 (63.3) 98 Moderate 4 (2.7) 142 (97.3) 146 Mild 1 (0.6) 168 (99.4) 169 Missing 0 11 11 PBI 8 66 74 5.66 (1.24, 25.75) 0.025 6 (60) 4 (40) 10 Severe 31 (96.9) 32 Moderate 1(3.1)Mild 1(3.1)31 (96.9) 32 Missing 0 0 3 20 23 16.11 (1.37, 189.11) 0.027 tICH 3 (37.5) 5 (62.5) 8 Severe Moderate 0 8 (100) 8 0 3 (100) 3 Mild 0 Missing 4 4

Odds ratio (OR) adjusted for age (0e13, 14e44, 45e65, >65 years); mechanism of injury (assault, road traffic accident, fall, other); and time to admission (<6, 6e12, 12e24, 24e72, 72e120, >120 hours).

CI, confidence interval; DSF, depressed skull fracture; ASDH, acute subdural hematoma; EDH, epidural hematoma; PBI, penetrating brain injury; tICH, traumatic intracerebral hematoma/contusion.

pressure probes, craniotomy for ASDH, and DC in other surgical series, particularly from high-income countries.<sup>31-34</sup>

Elevation of a DSF was the most frequent operation and associated with good postoperative outcomes, similar to a comparable report on DSF surgery.<sup>35</sup> DC was rarely performed and associated with the longest hospital stays, as previously reported.<sup>36</sup> In concordance with a Ugandan study, we found significant delays in time from admission to surgery, but almost 90% of patients with severe TBI were operated on within 24 hours of admission.<sup>37</sup> Other studies have shown time delays to be

95% CI for EXP (B) в SF Sig. Exp (B) Lower Upper 0.05 0.017 0.003 1.051 1.017 1.086 Age GCS score at admission -0.59 0.082 0.000 0.555 0.472 0.652 Time to admission -0.010 0.006 0.105 0.990 0.977 1.002 Length of stay -0.066 0.024 0.005 0.936 0.893 0.980 Logistic regression (Cox & Snell R<sup>2</sup> ¼ 20.2% and Nagelkerke R<sup>2</sup> ¼ 54.9). SE, standard of error; CI, confidence interval; EXP (B), exponentiation of B; GCS, Glasgow Coma Scale.

significantly associated with higher mortality rates.<sup>37,38</sup> In this study, we found that time from accident to admission was shorter for patients who died than for those who survived. We believe that this is a reflection of patient selection with a high mortality in the ED and the fact that less injured patients are more likely to survive prehospital delays.<sup>2-9</sup> Importantly, in a previous report from Black Lion Specialized Hospital in Addis Ababa, approximately 50% of patients with severe TBI died in the ED and only 62% of those who survived underwent operations.<sup>2</sup>

There are relatively few studies on surgical complications in TBI patients (most of these focus on DC), and these are difficult to compare due to major differences in data collection, definition, and presentation. The complication rate after elevation of a DSF was 12.8% with CSF leak being the most common complication. Other studies have reported higher complication rates, particularly wound infections.35,39 This difference might be related to antibiotic use, which was systematically used in our study. In another study from Addis Ababa, Salia et al40 reported dural tears in more than half of DSF patients. The high rate of postoperative CSF leak in our study was therefore probably related to difficulty of attaining a watertight closure of the dural defect (e.g., glue or dural substitutes were not available). The reoperation rate for ASDH patients in our series was 5.3%, which is lower than in a series of similar patients.<sup>41</sup> Overall, postoperative complications were seen in 17% of patients and 3% were reoperated on; these numbers were lower than anticipated given the resource limitations and patient selection in this study.

Patients with mild to moderate TBI usually had uneventful postoperative courses with good discharge outcomes. Studies from other LMICs have shown similar proportions of mild and moderate TBI with favorable outcome.<sup>42</sup> A study on TBI patient outcome comparing high-income countries (HICs) and LMICs showed that there was no difference in the odds of death in patients with mild and moderate TBI.<sup>42</sup> High age, short time to admission, low admission GCS score, ASDH, significant blood loss during surgery, postoperative complications, and long hospital stays were associated with unfavorable outcomes.

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The overall mortality rate was 8.2%. This was significantly lower than reported in a Malawian study43 but similar to a Ugandan study.31 The mortality rates for patients with a GCS score of 8 was higher (42.3%) than previously reported.44 Similar to other studies, we found admission GCS score to be a strong predictor of mortality.<sup>19,43</sup> Several reports on severe TBI have indicated that mortality in LMICs is higher than in HICs, and this can be attributed to lack of timely treatment and provision of care.<sup>31</sup> However, it is also important to keep in mind that the best decision for patients with severe injuries can be to withhold surgery, especially when elements like neuromonitoring and rehabilitation are completely missing. It is paramount in Ethiopian neurosurgical practice to not inflict an undue socioeconomic burden on the families of TBI survivors, and patients with an admission GCS score of 3e4 and/or fixed and dilated pupils are therefore generally not actively treated in the ICU or operated on.

In this study, we have reported several important outcome determinants, but we did not address critical factors such as hypoxemia and hypotension. Data on secondary insults were unfortunately to a large extent nonexistent, specifically in the prehospital setting. We chose to use GCS score at discharge as an outcome parameter. This was done to simplify data registration and make it easier to compare admission and discharge development. Moreover, it is difficult to track many of the patients after they have been discharged, particularly the most disabled. For ongoing projects, we have secured contact information and consent for more longitudinal follow-up data (e.g., Glasgow Outcome Scale). Finally, for a follow-up study, one needs to be aware of the risk of skewness toward a favorable outcome as many severely injured patients die before reaching definitive care or are never operated on.<sup>21</sup>

# CONCLUSIONS

Morbidity and mortality from trauma, particularly TBI, are enormous challenges for Ethiopian authorities and the entire health care system. More knowledge is needed to improve the quality of patient care and to further develop cost-effective neurosurgical services. In this study, we present surgical activity data and simple outcome measures for a large number of operated patients in the greater Addis region. These data and data presented elsewhere<sup>21</sup> clearly suggest that temporal delays and resource limitations in the continuum of care for TBI patients are associated with a significant patient selection that affects injury panorama, surgical activity, and patient outcome. This knowledge is important to guide current resource allocations, legislative programs, preventive initiatives, and neurosurgical management. There is still room for improvement before, during, and after hospital admission; nevertheless, many TBI patients in Ethiopia clearly benefit from surgical treatment and the surgical results presented here bear comparison to a large number of reports from HICs

#### CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Tsegazeab Laeke: Methodology, Writing - original draft, Formal analysis, Writing - review & editing. Abenezer Tirsit: Methodology. Azarias Kassahun: Methodology. Abat Sahlu: Investigation. Betelehem Yesehak: Investigation. Samuel Getahun: Investigation. Eyob Zenebe: Investigation. Negussie Deyassa: Formal analysis. Bente E. Moen: Writing - original draft. Morten Lund-Johansen: Methodology, Formal analysis, Writing - original draft. Terje Sundstrøm: Methodology, Writing - original draft, Formal analysis, Writing - review & editing.

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