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Prediction of early mortality after primary decompressive craniectomy in patients with severe traumatic brain injury

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Abstract

Objectives: Traumatic brain injury (TBI) is a worldwide major health problem associated with a high rate of morbidity and mortality. Intracranial hypertension following TBI is the main but not the only cause of early mortality. Decompressive craniectomy (DC) is used to decrease the intracranial pressure (ICP) and prevent brain herniation following TBI; however, the clinical outcome after DC for patients with TBI generates continuous debate. Prediction of early mortality after DC will help in making the surgery decision.

The aim of this study is to predict early mortality after DC based on the initial clinical and radiological findings.

Methods: In this study, 104 patients with severe traumatic brain injury have been treated by decompressive craniectomy and were retrospectively analyzed. Patients were divided into two groups; group I involved 32 patients who died within 28 days while group II involved 72 patients who survived after 28 days. The relationship between initial Glasgow Coma Scale score (GCS), pupil size and reactivity, associated injuries, and radiological findings were analyzed as predictor factors for early mortality.

Results: A total of 104 patients with severe TBI have been treated by DC and were analyzed; the early mortality occurred in 32 patients, 30.77%. There is a significant difference between groups in gender, mean GCS, Marshall scale, presence of isochoric pupils, and lung injury.

After stratification, odds of early mortality increases with the lower GCS, higher Marshall scale, lung injury, and abdominal injury while male gender and the presence of isochoric pupils decrease the odds of mortality. After univariate regression, the significant impact of GCS disappears except for GCS-8 which decreases the odds of mortality in comparison to other GCS scores while higher Marshall scale, presence of isochoric pupils, and lung injury increase the odds of mortality, but most of these effects disappear after multiple regressions except for lung injury and isochoric pupils.

Conclusion: Prediction of early mortality after DC is multifactorial, but the odds of early mortality after decompressive craniectomy in severe traumatic brain injury are progressively increased with the lower GCS, higher Marshall scale, and the presence of lung or abdominal injury.

Keywords: Traumatic brain injury, Decompressive craniectomy, Mortality, Outcome

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Introduction

Traumatic brain injury (TBI) is a worldwide major and challenging public health problem [1–4] with 39% global mortality [5]. TBI is considered one of the leading causes of death in pediatrics and adults less than 45 years [2]. Prediction of the mortality and functional outcome after severe traumatic brain injury TBI is an important but complicated subject.

In traumatic brain injury, the primary insult which involves the brain parenchyma or cerebral blood vessels is a physical insult due to the traumatic event that is not preventable while secondary brain insult which usually happens due to intracranial hypertension, brain ischemia, or seizures can be prevented [2]. It was found that post-traumatic intracranial hypertension not only increases the risk of mortality but is also considered the main cause of preventable death after traumatic brain injury [3, 6, 7].

Decompressive craniectomy (DC) had been described during the early years of the twentieth century for the treatment of intracranial hypertension and to prevent brain herniation [5, 8], becoming widely used as potentially life-saving procedures in cases with severe traumatic brain injury [2, 8–10]; however, there is still uncertainty regarding the effectiveness of DC on the outcome after TBI [11]. Despite the multiplicity and variability of the available studies in the literature, the results are conflicting and created a strong debate [3–12]. On the other hand, the ICP returns to normal level within 4 weeks after trauma [13], and according to this finding, decompressive craniectomy which decreases the ICP will modify the pathogenesis and can decrease the mortality during the initial 4 weeks of trauma.

In this study, demographic factors, initial clinical status, and radiological findings in addition to associated injuries were analyzed for the prediction of the early mortality after decompressive craniectomy aiming to help the neurosurgeons in the decision-making regarding the surgery and outcome expectations.

purpose

Prediction of the early mortality after decompression craniectomy was based on the initial clinical and radiological findings to facilitate the decision of to do or not to do DC after severe traumatic brain injury.

Methods

This is a retrospective cohort study that includes 104 patients who were admitted due to severe traumatic brain injury (Glasgow Coma Scale score ≤ 8) and have been treated with decompressive craniectomy at the Department of Neurosurgery, Zagazig University, and Kingdom Hospital in the period between 2013 and 2018.

All patients underwent a comprehensive clinical and radiological evaluation according to the advanced trauma life support guidelines (ATLS). All of them showed symptoms and signs of increased intracranial pressure with midline shift, compression of ventricular system, and basal cisterns with or without high or mixed density lesions $> 25 \text{ cm}^3$ in the initial computed tomography (CT) of the brain. All patients received an initial management in the emergency room and shifted directly after the primary and secondary survey to the operative theater while the postoperative care and follow-up were completed in the intensive care unit (ICU).

Patients with GCS-3 with bilaterally dilated non-reactive pupils, patients with Glasgow Coma Scale > 8 , patients with isolated extradural hematoma, patients with previous neurological deficit, patients with GCS-3, and those with incomplete data were excluded.

The study protocol was approved by the institutional review board at Zagazig University and the medical ethics committee of Kingdom Hospital.

The medical charts of the patients were reviewed for age, gender; early clinical condition, and brain CT scan findings. The Glasgow Coma Scale [14, 15] (Table 1) was used to classify the clinical status while pupils' size and reactivity were mentioned as an indicator for the brain stem function and the Marshall classification score of traumatic brain injury [16] was used to classify the radiological findings (Table 2).

Statistical analysis

Statistical analyses were carried out utilizing STATA. Data are summarized as mean \pm standard deviation (SD) and/or median with interquartile range and proportions as appropriate. Our primary outcome is 4 weeks mortality while the exposure variables are the initial GCS, size of pupils, extracranial-associated injuries, and Marshall CT brain grading.

In order to determine the outcome predictors, we compared the mean, median, or proportion between and survivors after 4 weeks and non-survivor using *t* test, chi-square, Wilcoxon test, and Kruskal-Wallis rank test while for the correlation between the exposure and outcome, univariate logistic regression was used while stratification and multivariate regression analysis were performed in order to eliminate the effects of confounders. A 2-sided *p* value of less than 0.05 was considered statistically significant.

Results

The study involved 104 patients, 92 male 88.5% and 12 females 11.5%; their mean age is 29.8 ± 14 and ranging between 4 and 66 years; the early mortality occurred in 32 patients 30.77% with statistically significant difference between survivors and non survivors in gender, mean

Table 1 Glasgow Coma Score (score of 13 or higher correlates with a mild brain injury, 9 to 12 is a moderate injury, and 8 or less a severe brain injury)

| | Best eye response | Best verbal response | Best motor response |
|---|-------------------------------|-------------------------|----------------------|
| 1 | No eye opening | No verbal response | No motor response |
| 2 | Eye opening to pain | Incomprehensible sounds | Extension to pain |
| 3 | Eye opening to verbal command | Inappropriate words | Flexion to pain |
| 4 | Eyes open spontaneously | Confused | Withdrawal from pain |
| 5 | | Orientated | Localizing pain |
| 6 | | | Obeys commands |

GCS score, mean Marshall scale, presence of isochoric pupils, and presence of lung injury, while age, left side lesion, orthopedic injury, and spinal injury did not show statistically significant difference between groups. The demographic, clinical, and radiological findings of the patients were summarized in Table 3.

Female gender, higher Marshall score, abdominal injury, and lung injury increased the odds of early mortality after decompressive craniectomy as odds of early mortality is 3 for GCS-3 with progressive decrease to lower level in patients with the higher GCS score even after regression analysis (Table 4) but without significant difference except for GCS-8 subgroup. Also there is significant correlation between risk of early mortality and Marshall scale (Table 4) as the odds of mortality increase from 0.6 to 3.1 with higher Marshall scale even after regression analysis, but this difference disappeared after multivariate logistic regression analysis (Table 5).

After multivariate regression analysis of the predictors for early mortality, only lung injury significantly increased the odds of mortality while female gender, increasing Marshall scale, or decreasing GCS has non-significant increase of the odds of mortality after decompressive craniectomy (Table 5).

After stratification of the patients, odds of early mortality increases with lower GCS (Fig. 1), higher Marshall scale (Fig. 2), lung injury, and abdominal injury while

male gender and presence of isochoric pupils decrease the odds of mortality (Table 4).

After univariate regression analysis, the odds of mortality increase with lower GCS score but without significant difference when $GCS \leq 7$ while odds of mortality for patients with GCS-8 is significantly lower than the odds of mortality for patient with $GCS \leq 7$. Also, after univariate regression analysis, the odds of early mortality are progressively increasing with higher Marshall scale (Table 4), but most of these effects disappear after multiple regressions except for lung injury, which increases the odds of mortality, and isochoric pupils, which decrease the odds of mortality (Table 4).

In this study, The most common surgery-related complications after DC are extra-axial fluid collection and hydrocephalus, wound infection, post-operative acute hematoma, and skin flap ischemia (Table 6), but there is no significant difference between groups except for extra-axial fluid collection (Fig. 3).

Discussion

Prediction of the outcome after severe traumatic brain injury (TBI) is a complicated subject as it is multifactorial depending on pre-trauma factors, nature of the trauma, post-traumatic events, and treatment [2, 3, 6, 7, 17]. For decades, investigators tried to build an outcome predictor model, but the results were contradicted due to the interaction between the different demographic, clinical, and radiological predictor factors. Gender, age, initial GCS, radiological findings, multiple injuries, and post-traumatic intracranial hypertension have been studied as prognostic factors with conflicting results [6, 7, 17–26], but there is agreement that post-traumatic intracranial hypertension is associated with increased mortality and poor outcome [3, 6, 7].

Intracranial hypertension during the first 48 h after traumatic brain injury (TBI) was found to be a predictor factor for mortality in patients with head injury [6], and recently, it was reported that ICP returns to normal level within 4 weeks from the trauma [13]. Decompressive craniectomy reduces the acute intracranial hypertension after severe traumatic brain injury [5, 8], but its impact on the outcome after TBI is still uncertain and debatable

Table 2 Marshall CT scale of traumatic brain injury

| Scale | CT findings |
|--------------|--|
| Category I | No visible intracranial pathology |
| Category II | Midline shift of 0 to 5 mm Basal cisterns remain visible No high or mixed density lesions >25 cm ³ |
| Category III | Midline shift of 0 to 5 mm Basal cisterns compressed or completely effaced No high or mixed density lesions > 25 cm ³ |
| Category IV | Midline shift > 5 mm No high or mixed density lesions > 25 cm ³ |
| Category V | Any lesion evacuated surgically |
| Category VI | High or mixed density lesions > 25 cm ³ Not surgically evacuated |

Table 3 Demographic and clinical findings of the patients

| | Cases with early mortality | Survived cases | p value |
|--|----------------------------|----------------|-----------|
| Number of patients | 32(30.77%) | 72(69.13%) | |
| Age | 28.1 ± 11.4 | 30.5 ± 15 | 0.4 |
| Gender | | | 0.004 |
| Male | 24(26%) | 68(74%) | |
| Female | 8(66.7%) | 4(33.3%) | |
| GCS | 4.6 ± 1.7 | 6.1 ± 1.9 | 0.0001*** |
| GCS-3 | 12(50%) | 12(50%) | 0.009*** |
| GCS-4 | 8(50%) | 8(50%) | |
| GCS-5 | 2(33.3%) | 4(66.7%) | |
| GCS-6 | 4(33.3%) | 8(66.7%) | |
| GCS-7 | 4(25%) | 12(75%) | |
| GCS-8 | 2(6.7%) | 28(93.3) | |
| Marshall scale | 5 ± 0.6 | 4.3 ± 0.99 | 0.0003*** |
| Marshall-3 | 1(4.2%) | 23(95.8%) | 0.006*** |
| Marshall-4 | 3(25%) | 9(75%) | |
| Marshall-5 | 23(39%) | 36(61%) | |
| Marshall-6 | 5(55.6%) | 4(44.4%) | |
| Pupils | | | |
| Dilated pupils | 4(40%) | 6(60%) | 0.5 |
| Constricted pupils | 8(25%) | 24(75%) | 0.3 |
| Isochoric pupils | 8(19%) | 34(80.9%) | 0.03* |
| Associated extra cranial injuries | | | |
| Spin injury | 8(40%) | 12(60%) | 0.3 |
| Abdominal injury | 8(100%) | 0 | 0.0001*** |
| Lung injury | 24(50%) | 24(50%) | 0.0001*** |
| Orthopedic injury | 4(20%) | 16(80%) | 0.2 |
| Left side lesion | 16(28.6%) | 40(71.4%) | 0.6 |

***denotes a highly significant statistical difference

Table 4 Odds of mortality after stratification and univariate regression analysis

| | Odds of mortality | p value | Odds ratio after univariate regression | p value |
|-----------------------|-------------------|---------|--|---------|
| GCS | | | | |
| GCS-3 | 3 | 0.02 | 1 | 1 |
| GCS-4 | 2.7 | 0.07 | 1 | 1 |
| GCS-5 | 1.1 | 0.8 | 0.5 | 0.47 |
| GCS-6 | 1.1 | 0.04 | 0.5 | 0.35 |
| GCS-7 | 0.7 | 0.5 | 0.3 | 0.12 |
| GCS-8 | 0.1 | 0.0007* | 0.07 | 0.002* |
| Marshall scale | | | | |
| Marshall-3 | 0.07 | 0.001* | 0.04 | 0.002* |
| Marshall-4 | 0.7 | 0.6 | 7.6 | 0.09 |
| Marshall-5 | 2.6 | 0.03* | 14.7 | 0.01** |
| Marshall-6 | 3.1 | 0.09* | 28.7 | 0.006** |

*denotes mild statistically significant difference

**denotes moderate statistically significant difference

Table 5 Odds of mortality after multiple regression

| Early mortality | Odds ratio | Std. Err. | z | p value | 95% confidence interval | |
|-----------------------|------------|-----------|--------|---------|-------------------------|--------|
| GCS | | | | | | |
| GCS-4 | 8.72 | 14.9 | 1.27 | 0.2 | 0.30 | 246.74 |
| GCS-5 | 0.31 | 0.41 | - 0.89 | 0.4 | 0.03 | 3.95 |
| GCS-6 | 0.08 | 0.12 | - 1.69 | 0.09 | 0.01 | 1.48 |
| GCS-7 | 0.07 | 0.10 | - 1.85 | 0.06 | 0.01 | 1.16 |
| GCS-8 | 0.17 | 0.31 | - 0.97 | 0.33 | 0.01 | 6.1 |
| Marshall scale | | | | | | |
| Marshall-4 | 55.57 | 118.67 | 1.88 | 0.06 | 0.85 | 3651.8 |
| Marshall-5 | 22.24 | 37.31 | 1.85 | 0.06 | 0.83 | 595.7 |
| Marshall-6 | 8.22 | 17.39 | 1 | 0.31 | 0.13 | 517.3 |
| Female gender | 6.16 | 6.17 | 1.81 | 0.07 | 0.86 | 43.9 |
| Isochoric pupils | 0.04 | 0.05 | - 2.4 | 0.02* | 0.003 | 0.553 |
| Lung injury | 17.05 | 23.57 | 2.05 | 0.04* | 1.13 | 256.00 |
| _cons | 0.19 | 0.06 | - 1.77 | 0.48 | 0.002 | 19.7 |

*a mild statistically significant difference

subject [3, 11]. In this study, Out of the 104 patients, early mortality was detected in 32 patients 30.77% which is lower than mortality in other studies as it was 43% in the series of Grille and Tommasino [5] and 37.6% in the study of Katznelson et al. [19], but the mortality in this study is higher than the mortality in one of the most famous and recent randomized trial of decompressive craniectomy for traumatic intracranial hypertension which was 26.9% in the surgical arm [9], and this may be due to the timing of intervention or the nature of trauma as in our series, most of the patient were involved in motor vehicle accident and were treated after

6 h due to delayed transfer from the scene of the trauma.

Old age is usually associated with poor outcome after TBI [20], but in this study, the mean age of patients is 29.8 ± 14 years with interquartile range between 21 and 35 years (Fig. 1) without significant difference between survivors and non-survivors (Table 3).

In this study, 92 males and 12 females had severe traumatic brain injury with significant difference between groups as the early mortality was reported in 66.67% of the female patients while in male patients, it was only

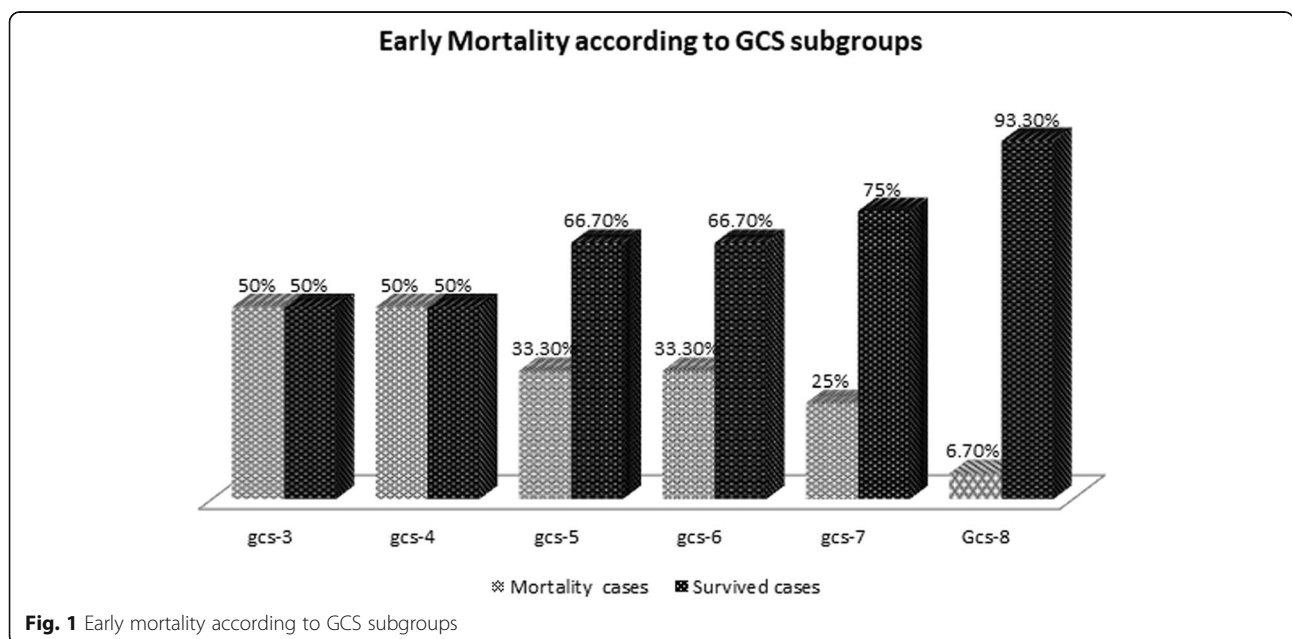


Fig. 1 Early mortality according to GCS subgroups

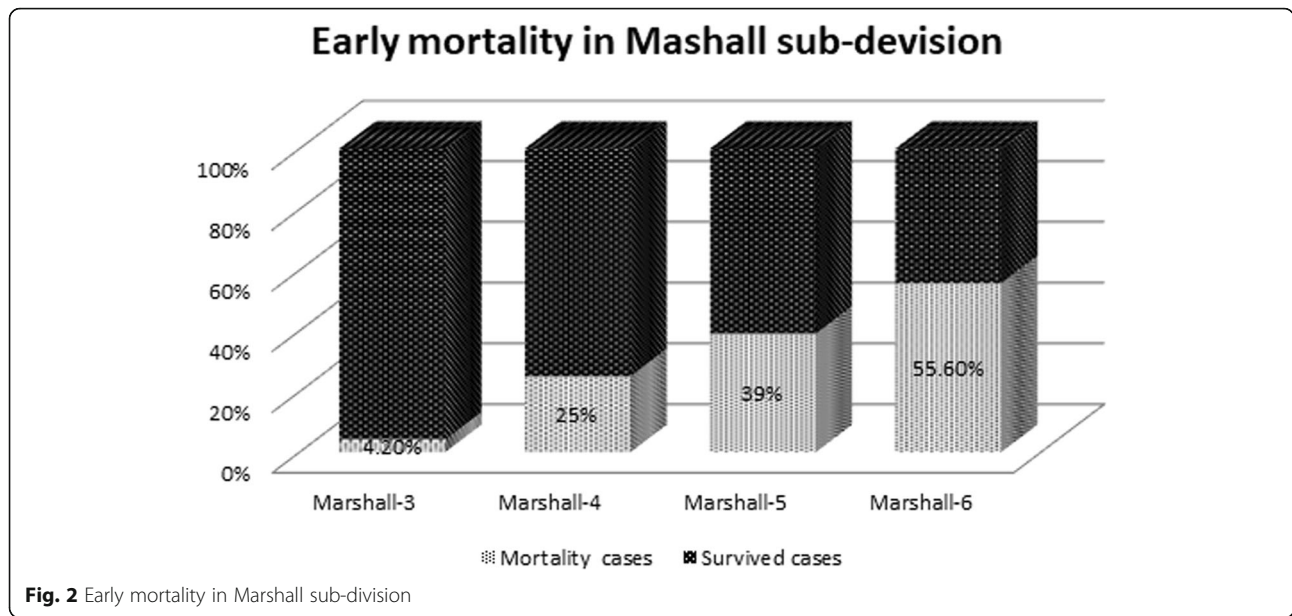


Fig. 2 Early mortality in Marshall sub-division

26.1%, and this findings is in agreement with several older studies which reported that outcome after TBI is poorer in women than men, [21, 23, 24] but in apparent disagreement was found in other studies which showed no differences in either acute complications or outcome after TBI between males and females [25, 26].

Glasgow Coma Scale (GCS) is the standardized scale for measurement of neurological status in TBI [18] and significant correlation with outcome after severe TBI had been reported [17, 19, 27] as it was reported that patients with low GCS on admission have poor prognosis and usually correlates with mortality [18], and the overall mortality in patients with initial GCS-3 was 76% [28]. In the current study, significant difference was observed in the mean value of GCS between survivors and non-survivors (Table 1) and the early mortality in patient with GCS-3 is 50% and the odds is 3 (Table 4) with significant reduction of the odds of mortality with the increase in GCS (Fig. 1) but multivariate regression analysis reduce the effect of GCS on the risk of early mortality (Table 5). These results are in agreement with Kodliwadmth et al. [29] who concluded that GCS can

stratify the risk and prognosis in patients with traumatic brain injury but with caution in patients with poly-trauma as other injuries can modify the morbidity and mortality; also, in another study, the initial neurological status measured by the GCS reflects the severity of brain injury but not associated with mortality [19].

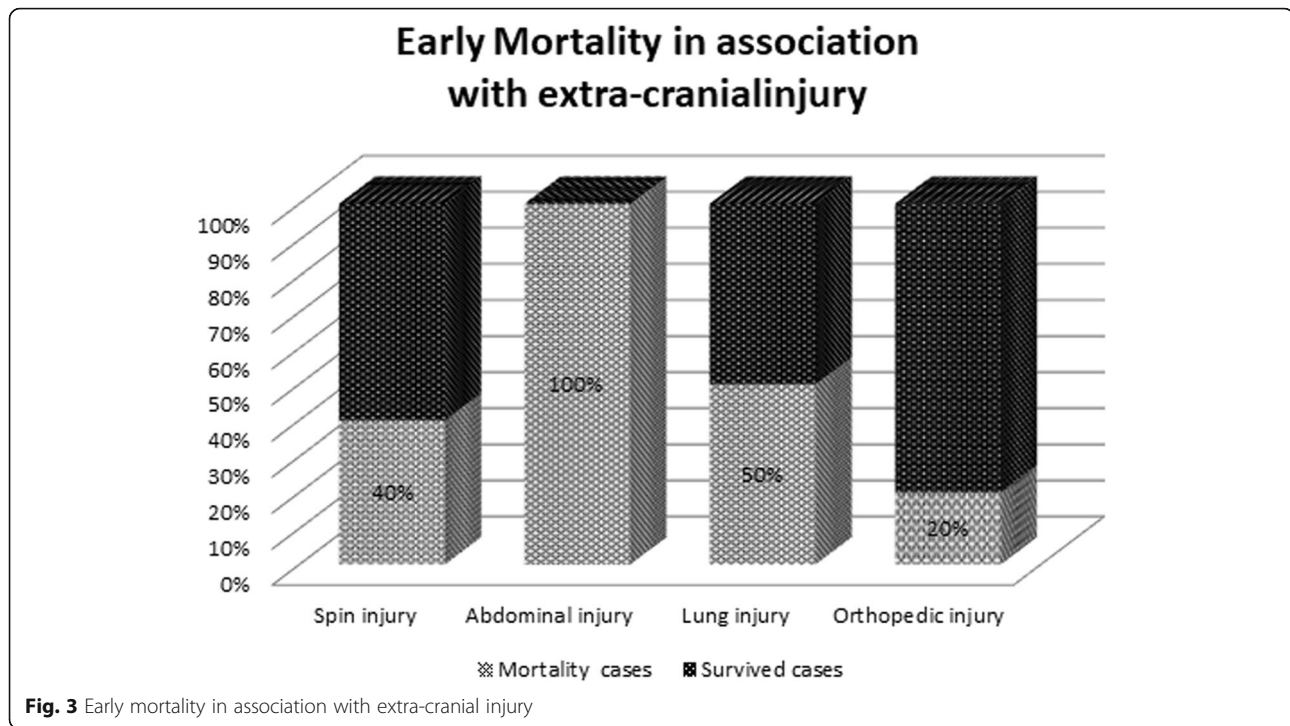
Pupil examination is very important during the clinical evaluation of the patients with TBI and the pupil size and reactivity are significant predictors of mortality in patient with low GCS [30]. In our study, the pupil examination was stratified into normal, constricted, isochoric, and dilated but reactive while patients with dilated non-reactive pupils were excluded and only isochoric pupils is the only type of pupils that showed significant difference between survivors and non-survival even after multiple regression as it decreases the odds of mortality.

Initial radiological evaluation can predict the outcome in patients with TBI [31]. The Marshall CT classification is one of the most common radiological predictors for the outcome after TBI and higher score was found significantly associated with early mortality after TBI, and Katznelson et al. [19] reported similar

Table 6 Surgery-related complication after decompressive craniectomy

| | Total (104) | Mortality (32) | No mortality (72) | p value |
|-------------------------------|-------------|----------------|-------------------|----------|
| Hydrocephalus | 11 (10.6%) | 1 (3.1%) | 10 (13.9%) | 0.16 |
| Extra-axial fluid collection | 20 (19.2%) | 2 (6.3%) | 18 (25%) | 0.005*** |
| Post-operative CSF leak | 6 (5.8%) | 3 (2.9%) | 3 (4.2%) | 0.7 |
| Wound infection | 6 (5.8%) | 3 (2.9%) | 3 (4.2%) | 0.7 |
| Post-operative acute hematoma | 8 (7.7%) | 5 (15.6%) | 5 (4.2%) | 0.08 |
| Skin flap ischemia | 5(4.8%) | 3 (9.4%) | 2 (2.8%) | 0.5 |

***denote a highly significant statistical difference



results as high Marshall score was associated with higher rate of early mortality even after logistic regression. In the current study, the mean value of Marshall scoring system was higher in the non-survivor group than survivor with statistical increase in the odds of mortality with higher score (Fig. 2), but this difference is reduced to non-significant level after multivariate analysis. This finding is in agreement with other recent studies as no significant correlation between mortality and Marshall CT classification score during the first 2 weeks and the first month or at the third month [32].

Associated extracranial injuries modify the outcomes of traumatic brain injury [33–35], but the results of clinical studies are contradicted as it leads to increases in patient mortality [33, 35] while other investigators concluded that the extra cranial injury has little or no effect on the outcome [4, 36]. In our study, presence of extra cranial injury increases the risk of early mortality (Table 1), and lung injury and abdominal injury with internal hemorrhage were strong predictors for early mortality after decompressive craniectomy while spine and orthopedic injuries did not modify the odds of early mortality, and this can be explained by the associated hypotension and/or hypoxia in cases with abdominal trauma and lung injury respectively.

Surgery-related complications after DC involve cerebral hematoma which may be due to blooming of contusions or newly developed contralateral acute subdural

hematoma, surgical wound infection, sunken flap, and hydrocephalus [8, 37], and in this study, the most common surgery-related complications after DC are extra-axial fluid collection and hydrocephalus, wound infection, post-operative acute hematoma, and skin flap ischemia (Table 6), but there is no significant difference between groups except for extra-axial fluid collection.

Conclusion

The odds of early mortality after DC in patients with severe traumatic brain injury are progressively increasing with the lower GCS, higher Marshall scale, and the presence of lung or abdominal injury, but early mortality is multifactorial and DC is still an option of treatment for all patients with severe traumatic brain injury.

Abbreviations

DC: Decompressive craniectomy; TBI: Traumatic brain injury; GCS: Glasgow Coma Scale; ATLS: Advanced Trauma Life Support; ICP: Intracranial pressure; CT: Computed tomography

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Authors' contributions

SA was a major contributor in writing the manuscript and analyzed and interpreted the patient data. AA contributed in collecting data and writing the manuscript. SE was a major contributor in writing the manuscript and participating in the collection of the data. FF was responsible for the interpretation of radiological findings. SE was a major contributor in writing the manuscript and OK contributed in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the Ethical standards of the institutional and/or national research committee (Zagazig Faculty of Medicine IRP committee and Kingdom Hospital ethical committee) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethical committee at Kingdom Hospital gave the ethical approval on November 7, 2018 while *consent to participate* is not applicable for this type of study and formal consent is not required.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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