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Original Article

Post-traumatic decompressive craniectomy: Prognostic factors and long-term follow-up

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ABSTRACT

Background: Decompressive craniectomy (DC) is still controversial in neurosurgery. According to the most recent trials, DC seems to increase survival in case of refractory intracranial pressure. On the other hand, the risk of postsurgical poor outcomes remain high. The present study aimed to evaluate a series of preoperative factors potentially impacting on long-term follow-up of traumatic brain injury (TBI) patients treated with DC.

Methods: We analyzed the first follow-up year of a series of 75 TBI patients treated with DC at our department in five years (2015–2019). Demographic, clinical, and radiological parameters were retrospectively collected from clinical records. Blood examinations were analyzed to calculate the preoperative neutrophil-to-lymphocyte ratio (NLR). Disability rating scale (DRS) was used to classify patients' outcomes (good outcome [G.O.] if DRS ≤11 and poor outcome [P.O.] if DRS ≥12) at 6 and 12 months.

Results: At six months follow-up, 25 out of 75 patients had DRS ≤11, while at 12 months, 30 out of 75 patients were included in the G.O. group. Admission Glasgow Coma Scale (GCS) >8 was significantly associated with six months G.O. Increased NLR values and the interval between DC and cranioplasty >3 months were significantly correlated to a P.O. at 6- and 12-month follow-up.

Conclusion: Since DC still represents a controversial therapeutic strategy, selecting parameters to help stratify TBI patients' potential outcomes is paramount. GCS at admission, the interval between DC and cranioplasty, and preoperative NLR values seem to correlate with the long-term outcome.

Keywords: Cranioplasty, Decompressive craniectomy, Neutrophil-to-lymphocyte ratio, Outcome, Traumatic brain injury

INTRODUCTION

According to the most recent clinical trials,[8,19] decompressive craniectomy (DC) effectiveness in severe traumatic brain injury (TBI) is mostly limited to gain control of raised intracranial pressure (ICP), when refractory to maximal medical treatment. Under such conditions, surgery mainly seems to increase survival at the expense of an increased number of patients remaining in poor neurological conditions.[17] This consideration and the complexity of postoperative management help explain some authors' adversity to cranial decompression.

Our study aimed to reconsider the long-term follow-up of TBI patients treated by DC over five years at our institution, thoroughly analyzing a series of preoperative clinical, radiological, and hematological factors potentially impacting patients' prognosis with the aim of a successful case selection.

MATERIALS AND METHODS

We analyzed retrospectively the first follow-up year of a series of 75 TBI patients treated with DC and subsequent cranioplasty at our department from January 2015 to December 2019.

Gender, age, comorbidities (hypertension, diabetes mellitus [DM], and use of antiplatelet drug), Glasgow Coma Scale (GCS), and Rotterdam Scores (RS) were assessed in all patients at admission; full blood count was also obtained to establish the neutrophil-to-lymphocyte ratio (NLR). Clinical outcomes at 6 and 12 months were evaluated by the disability rating scale (DRS) through direct or telephonic interviews with the patients or their family members. Based on their final DRS, subjects were classified into two main classes, respectively, "good outcome group" (G.O., no or moderate disability, [DRS 0-11]) and "poor outcome group" (P.O., severe disability or dead [DRS 12–30]). Finally, the interval time between craniectomy and cranioplasty was also considered. For each patient, the follow-up time after cranioplasty was 18 months. Nontraumatic patients, subjects <16 years of age or with previous craniotomy, known compromised cognitive and motor performance subsequent to previous neurological damage from different causes were excluded from the study.

Data analysis was performed using the STATA/IC 13.1 statistical package (StataCorp LP, Texas, USA). Values are presented as the median (interquartile range) for continuous variables and the number (percent) of subjects for categorical variables. Univariate comparison was made through the Mann–Whitney test or Chi-squared test, as appropriate. The association between baseline characteristics and 6- and 12-month functional outcomes was determined using logistic regression analysis. Results were considered significant for $P < 0.05$ (two-sided).

RESULTS

Over the considered period, given the exclusion criteria, 75 TBI patients were treated with DC over the considered period, of which 62 men (82.7%) and 13 women (17.3%) were enrolled in the current study.

Comorbidities were distributed as follows: 27 patients (36%) suffered from hypertension, 33 patients (44%) from DM, and 15 patients (20%) were on antiplatelet drugs.

The findings identified on computed tomography (CT) performed on arrival at the emergency department were as follows: 41% of patients presented with acute subdural hematoma, 35% with hemorrhagic contusions, 14% with epidural hematoma, and 10% with diffuse cerebral edema.

At six months follow-up, the G.O. consisted of 25 out of 75 patients, while at 12 months follow-up, the same group was composed of 30 out of 75 subjects.

Table 1: Baseline characteristics of patients according to 6-month outcome.

	Good outcome (DRS 0-11) (*n*=25)	Poor outcome (DRS 12-30) (*n*=50)	*P* value
Age >40 years	13 (52.0)	31 (62.0)	0.407
Male sex	19 (76.0)	43 (86.0)	0.281
Baseline GCS >8	17 (68.0)	1 (2.0)	**<0.001**
Rotterdam score >3	1 (4.0)	35 (70.0)	**<0.001**
Time to repositioning of cranial bone flap >3 months	1 (4.0)	43 (86.0)	**<0.001**
Neutrophil-to-lymphocyte ratio	1.86 (1.22-2.56)	3.95 (2.65-4.91)	**<0.001**

GCS: Glasgow coma scale, DRS: Disability rating scale, Bold indicates the statistical significative results.

Table 2: Baseline characteristics of patients according to 12-month outcome.

	Good outcome (DRS 0-11) (*n*=30)	Poor outcome (DRS 12-30) (*n*=45)	*P* value
Age >40 years	16 (53.3)	28 (62.2)	0.444
Male sex	24 (80.0)	38 (84.4)	0.618
Baseline GCS >8	17 (56.7)	1 (2.2)	**<0.001**
Rotterdam score >3	3 (10.0)	33 (73.3)	**<0.001**
Time to repositioning of cranial bone flap >3 months	3 (10.0)	41 (91.1)	**<0.001**
Neutrophil-to-lymphocyte ratio	1.86 (1.22-2.58)	4.10 (2.87-4.96)	**<0.001**

GCS: Glasgow coma scale, DRS: Disability rating scale, Bold indicates the statistical significative results.

Table 3: Association of baseline characteristics with 6-month poor outcome (DRS 12-30).

Independent variable	Unadjusted		Adjusted	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age >40 years	1.51 (0.57-3.97)	0.408	1.24 (0.14-11.28)	0.850
Male sex	1.94 (0.57-6.55)	0.286	0.29 (0.01-8.45)	0.470
Baseline GCS score <8	0.01 (0.001-0.08)	<0.001	0.03 (0.001-0.53)	**0.018**
Rotterdam score >3	56.00 (6.93-452.68)	<0.001	3.39 (0.07-162.53)	0.537
Time to repositioning of cranial bone flap >3 month	147.43 (17.10-1270.70)	<0.001	64.8 (1.43-2941.76)	**0.032**
Increased Neutrophil-to- lymphocyte ratio	3.38 (1.86-6.13)	<0.001	9.18 (1.07-78.67)	**0.043**

GCS: Glasgow coma scale; OR: Odds ratio, CI: Confidential interval. Bold indicates the statistically significant results

Table 4: Association of baseline characteristics with 12-month poor outcome (DRS 12-30).

Independent variable	Unadjusted		Adjusted	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age >40 years	1.44 (0.56-3.68)	0.445	1.16 (0.19-7.11)	0.876
Male sex	1.36 (0.41-4.52)	0.619	0.24 (0.01-4.51)	0.337
Baseline GCS score <8	0.02 (0.002-0.14)	<0.001	0.13 (0.01-2.24)	0.160
Rotterdam score >3	24.75 (6.33-96.77)	<0.001	0.36 (0.02-6.49)	0.492
Time to repositioning of cranial bone flap >3 month	92.25 (19.12-445.10)	<0.001	47.18 (3.07-726.00)	**0.006**
Increased Neutrophil-to- lymphocyte ratio	3.27 (1.88-5.68)	<0.001	2.75 (1.13-6.69)	**0.025**

GCS: Glasgow coma scale; OR: Odds ratio, CI: Confidential interval. Bold indicates the statistically significant results

The data analyzed and compared between patients with G.O. and P.O. at 6 and 12 months are illustrated in Tables 1 and 2. Tables 3 and 4 show the association between baseline characteristics and functional outcomes at 6 and 12 months.

Neither age nor gender resulted significantly in statistical analysis.

Admission GCS <8 was a significant predictor of P.O. both at 6- and at 12-month follow-up at the univariate analysis. However, this finding maintained its statistical significance in the multivariate analysis only at 6-month follow-up. ($P = 0.018$).

Although high RS resulted in a significant predictor of P.O. at the univariate analysis at 6 and 12 months follow-up, the multivariate analysis did not confirm its statistical significance.

A time interval >3 months between the DC and the bone flap repositioning resulted in a statistically significant parameter associated with P.O. at 6- and 12-month follow-up (6 months $P = 0.032$; 12 months $P = 0.006$).

The NLR was significantly higher in P.O. patients than G.O.; in particular, mean NLR was, respectively, 3.95 (range, 2.65–4.91) and 1.86 (range, 1.22–2.56) at 6-month follow-up and 4.10 (range, 2.87–4.96) and 1.86 (range, 1.22–2.58) at 12-month follow-up. The statistical significance of this finding was confirmed at multivariate analysis (6 months $P = 0.04$; 12 months $P = 0.003$).

DISCUSSION

Indications to DC for intractable ICP remain a controversial matter. Technical aspects, timing of surgery, and patient selection are continuously debated in the neurosurgical community.[19,20,23] Moreover, concerns are still related to the potential early and late postsurgical complications and the risk of a poor long-term outcome for patients treated with DC.[7]

According to the most recent Brain Trauma Foundation guidelines,[19] integrating the updated RESCUEicp,[7] and the DECRA[9] trial results, secondary DC is suggested to resolve refractory intracranial hypertension and to reduce intensive care management duration. Unfortunately, no trial provides a definitive conclusion, and what clearly emerges from the literature is that the decision of whether to perform or not DC depends on a case-by-case basis, evaluating the risks and benefits of the surgical procedure and attempting to predict the potential functional outcome of the patient in question. However, despite the technical advances, this attempt remains extremely arduous. Hence, it is evident the importance of establishing which parameters have a significant predictive value on the outcome of these patients.

Conventionally, clinical parameters such as age, admission GCS, pupillary response, and radiological assessment have helped neurosurgeons to guide the decision.[21] Moreover, different models (e.g., Marshall CT score, Rotterdam CT score, and the International Mission for Prognosis and Analysis of Clinical Trials [IMPACT] and Corticosteroid Randomization After Significant Head injury [CRASH] models) have been used to estimate the neurological outcome and predict mortality in TBI patients.[4]

Sahuquillo and Dennis' Cochrane Review[35] investigated the neurological outcome and survival of closed TBI patients treated with DC or the sole standard medical care. The review underlined the superiority of DC in lowering ICP within 48 h and in reducing the mortality at 6 and 12 months follow-up compared to medical treatment alone. However, whether or not DC may lead to a beneficial effect on the long-term neurological outcome, compared to the standard medical care alone, remained unclear.

In our series, the male sex was predominant, constituting 82.7% of the whole population sample and corroborating the results of the epidemiologic studies on TBI.[2,32] As the literature reports, gender did not affect the neurological outcome in our series.[18]

Although age is a well-known TBI prognostic parameter,[12,30] our analysis did not show a clearly association between age >40 years and a worst six or 12-month outcome, but this may be due to a bias related to the small sample examined.

The evaluation of the admission GCS score is paramount to predicting the potential neurological result of a surgical procedure.[24,30] In our investigation, initial GCS <8 demonstrated to be a reliable predictor factor for 6 and 12 months P.O. at the univariate analysis,[26,28] although unconfirmed at the multivariate analysis at 12 months follow-up.

A possible bias in our study could be the delay in surgery due to the transport time from remote areas. After admission to our hospital, that is the only level III trauma center in the region, there was no delay in surgery timing.

The Rotterdam Scoring System helps to estimate the posttrauma 6-month prognosis and mortality using radiological criteria.[4,22]

In our series, an RS >3 was found in the 70% and the 73.3% of P.O. patients, respectively, at 6 and 12 months follow-up. This was largely expected since RS increases with the severity of the radiological findings. Nevertheless, the statistical significance of this parameter as an independent prognostic factor for TBI was not confirmed at the multivariate analysis both at six and at 12 months follow-up.

Cranioplasty is another important issue related to DC: the correct timing to perform it, the selection of the most suitable material to reduce/avoid complications (e.g., infections, seizures, bone flap resorption, hydrocephalus, hemorrhage, and cosmetic issues), the storage/fixation techniques are still controversial.[1,13,36] Our study focused on whether an early (<3 months) cranioplasty surgery could lead or not to a better long-term outcome.

The optimal timing of cranioplasty is still ill-defined: some authors[10,33] state that the repair of the skull defect leads to a neurological improvement, no matter when such surgery is performed, while others[25,29] affirm that early cranioplasty could determine a greater neurological improvement after a TBI. On the counterpart, some studies show that early cranioplasty would produce a higher complication rate.[3,16]

In the present study, cranioplasty performed after three or more months from DC result associated with P.O. at 6- and 12-month follow-up.

This finding could be explained by the assumption that the earlier the cranioplasty, the earlier the restoration of some potential abnormalities caused by the DC (e.g., cerebrospinal fluid dynamics disturbances, altered cerebral perfusion, and metabolic rate of oxygen and glucose).[31]

Moreover, cranioplasty can help to prevent/solve eventual syndromes which may complicate the postoperative recovery after DC (e.g., Syndrome of the trephined and craniectomy-associated progressive extra-axial collections with treated hydrocephalus).[40]

Recently, researchers have focused on the prognostic role of the systemic inflammatory response in neurological diseases and trauma, with the intent of increasing the accuracy of the already existing prognostic models such as CRASH and IMPACT.[21]

NLR is now a worldwide accepted significant index of inflammation, and its value in predicting the outcome after a TBI is widely discussed in the literature. Its advantages over the other prognostic factors lie in the ease of obtaining, the low cost, and the objectivity of the datum.

Over the past years, several studies have suggested a correlation between the increase in admission NLR and the P.O. of various diseases, including TBI.[5,27]

Chen *et al*.[6] conducted a retrospective study on 688 patients with severe TBI, of which 508 had an unfavorable prognosis. They found that admission NLR was higher in patients with P.O., compared to those with a good recovery, and that a higher NLR was statistically associated with higher 1-year mortality. The authors stated that NLR is a significant independent parameter in predicting TBI's functional outcome and mortality.

Siwicka-Gieroba *et al*. [37] performed a study on a series of 144 patients affected by severe TBI. They concluded that higher admission NLR values seemed to predict worse outcomes, and a value >15.63 would be a predictor of 28-day mortality.

Zhao *et al*.[39] conducted a retrospective study on a sample of 1291 subjects affected by TBI to assess whether the NLR was or not an independent prognostic parameter for the six-month outcome of these patients. They found significantly higher NLR values in patients with P.O., compared to those with good prognosis, and concluded that NLR can be considered as an independent prognostic factor in TBI.[38]

On the contrary, Corbett *et al*.[11] retrospectively analyzed 388 severe TBI patients treated with DC, of which 151 with P.O. at 18 months follow-up, and found that NLR was not significantly

higher in the latter. Moreover, none of the hematological parameters taken into consideration supplemented the IMPACT model in predicting the long-term neurological outcome. Dolmans *et al*.[14] investigated the prognostic value of routine admission blood tests, including NLR, in 255 patients with severe TBI, but they found no statistical association between the hematological parameters and the prognosis/mortality of the subjects enrolled in their study.

A recent review conducted by Sabouri *et al*.[34] concluded that a higher NLR value correlates with a lower GCS score and could be a good prognostic factor in predicting functional outcomes and mortality in patients with severe TBI.

In this complex picture, the results of our study seem to corroborate the hypothesis that admission NLR value could help to stratify the long-term outcome in TBI patients. In fact, in the P.O., the mean admission NLR was higher than in the G.O. This difference was significant in both the univariate and multivariate analysis.

However, it is important to underline that the values found in our investigation were not particularly high in both groups, even if the mean NLR exceeded the healthy adults cutoff value (3.53)[15] only in the P.O.

Nonetheless, the NLR values found in our study are much lower than those indicated by Chen *et al*. (13.05)[6] and Siwicka-Gieroba *et al*. (15.63)[37] as predictors for P.O./mortality in TBI. There are several limits in this study. In particular, the retrospective nature and the small size of the sample analyzed make it vulnerable to biases. In addition, the dichotomization of the outcome groups was made based on the DRS (0–11/12–30), including patients with moderately severe disability in the G.O. and those with severe disability in the P.O. Therefore, our results should be interpreted with caution and further studies are needed to confirm our conclusion.

CONCLUSION

The selection of parameters that can help stratify TBI patients' potential outcomes is paramount. In our study, the GCS, the timing of the cranioplasty, and the admission NLR resulted in independent predictor factors associated with the 6-month outcome, while only the timing of the cranioplasty and the NLR significantly correlated with the 12-month outcome of patients treated with DC due to a TBI.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Our Local Ethics Committee waived ethical approval in view of the study's retrospective nature, and all the procedures being performed were part of the routine care.

Data availability

Patients and their families were assured that data would remain confidential and would not be shared.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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