JAMA Neurology | Original Investigation

Evaluation of Outcomes Among Patients With Traumatic Intracranial Hypertension Treated With Decompressive Craniectomy vs Standard Medical Care at 24 Months

A Secondary Analysis of the RESCUEicp Randomized Clinical Trial

Angelos G. Kolias, MD, PhD; Hadie Adams, MD; Ivan S. Timofeev, PhD; Elizabeth A. Corteen, MSc; Iftakher Hossain, MD, PhD; Marek Czosnyka, PhD; Jake Timothy, MD; Ian Anderson, MB ChB; Diederik O. Bulters, MB ChB; Antonio Belli, MD; C. Andrew Eynon, MD; John Wadley, MB ChB; A. David Mendelow, MB ChB, PhD; Patrick M. Mitchell, MB BChir, PhD; Mark H. Wilson, MB BChir, PhD; Giles Critchley, MD; Juan Sahuquillo, MD, PhD; Andreas Unterberg, MD, PhD; Jussi P. Posti, MD, PhD; Franco Servadei, MD; Graham M. Teasdale, MD; John D. Pickard, MD; David K. Menon, MB BS, PhD; Gordon D. Murray, PhD; Peter J. Kirkpatrick, MB ChB; Peter J. Hutchinson, MB BS, PhD; for the RESCUEicp Trial Collaborators

IMPORTANCE Trials often assess primary outcomes of traumatic brain injury at 6 months. Longer-term data are needed to assess outcomes for patients receiving surgical vs medical treatment for traumatic intracranial hypertension.

OBJECTIVE To evaluate 24-month outcomes for patients with traumatic intracranial hypertension treated with decompressive craniectomy or standard medical care.

DESIGN, SETTING, AND PARTICIPANTS Prespecified secondary analysis of the Randomized Evaluation of Surgery With Craniectomy for Uncontrollable Elevation of Intracranial Pressure (RESCUEicp) randomized clinical trial data was performed for patients with traumatic intracranial hypertension (>25 mm Hg) from 52 centers in 20 countries. Enrollment occurred between January 2004 and March 2014. Data were analyzed between 2018 and 2021. Eligibility criteria were age 10 to 65 years, traumatic brain injury (confirmed via computed tomography), intracranial pressure monitoring, and sustained and refractory elevated intracranial pressure for 1 to 12 hours despite pressure-controlling measures. Exclusion criteria were bilateral fixed and dilated pupils, bleeding diathesis, or unsurvivable injury.

INTERVENTIONS Patients were randomly assigned 1:1 to receive a decompressive craniectomy with standard care (surgical group) or to ongoing medical treatment with the option to add barbiturate infusion (medical group).

MAIN OUTCOMES AND MEASURES The primary outcome was measured with the 8-point Extended Glasgow Outcome Scale (1 indicates death and 8 denotes upper good recovery), and the 6- to 24-month outcome trajectory was examined.

RESULTS This study enrolled 408 patients: 206 in the surgical group and 202 in the medical group. The mean (SD) age was 32.3 (13.2) and 34.8 (13.7) years, respectively, and the study population was predominantly male (165 [81.7%] and 156 [80.0%], respectively). At 24 months, patients in the surgical group had reduced mortality (61 [33.5%] vs 94 [54.0%]; absolute difference, −20.5 [95% CI, −30.8 to −10.2]) and higher rates of vegetative state (absolute difference, 4.3 [95% CI, 0.0 to 8.6]), lower or upper moderate disability (4.7 [−0.9 to 10.3] vs 2.8 [−4.2 to 9.8]), and lower or upper severe disability (2.2 [−5.4 to 9.8] vs 6.5 [1.8 to 11.2]; $\chi^2_7 = 24.20$, $P = .001$). For every 100 individuals treated surgically, 21 additional patients survived at 24 months; 4 were in a vegetative state, 2 had lower and 7 had upper severe disability, and 5 had lower and 3 had upper moderate disability, respectively. Rates of lower and upper good recovery were similar for the surgical and medical groups (20 [11.0%] vs 19 [10.9%]), and significant differences in net improvement (≥1 grade) were observed between 6 and 24 months (55 [30.0%] vs 25 [14.0%]; $\chi^2_2 = 13.27$, $P = .001$).

CONCLUSIONS AND RELEVANCE At 24 months, patients with surgically treated posttraumatic refractory intracranial hypertension had a sustained reduction in mortality and higher rates of vegetative state, severe disability, and moderate disability. Patients in the surgical group were more likely to improve over time vs patients in the medical group.

TRIAL REGISTRATION ISRCTN Identifier: 66202560

JAMA Neurol. 2022;79(7):664-671. doi:10.1001/jamaneurol.2022.1070
Published online June 6, 2022.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Angelos G. Kolias, MD, PhD, Department of Clinical Neurosciences, University of Cambridge, Box 167, Biomedical Campus, Cambridge CB2 0QQ, United Kingdom (ak721@cam.ac.uk).

Decompressive craniectomy is a life-saving procedure to reduce critically elevated intracranial pressure (ICP) among patients with traumatic brain injury (TBI).[1] The optimal timing, indications, and functional outcome benefits associated with decompressive craniectomy have been widely debated.[2] Two multicenter randomized clinical trials, Decompressive Craniectomy (DECRA) and Randomized Evaluation of Surgery With Craniectomy for Uncontrollable Elevation of Intracranial Pressure (RESCUEicp), have reported contradictory findings.

The DECRA trial, published in 2011, assessed early decompressive craniectomy for patients with diffuse TBI who experienced increased ICP (>20 mm Hg for >15 minutes within 1 hour) despite optimized early interventions such as sedation, normalized arterial carbon dioxide pressure, and use of hyperosmolar therapy, neuromuscular blockade, and external ventricular drainage.[3] DECRA patients were randomized to (1) early bifrontal decompressive craniectomy and standard care or (2) standard care. In 2013, the DECRA investigators reported similar mortality rates and a higher rate of unfavorable outcomes for patients who received a decompressive craniectomy at 6 months vs those who received standard care.[4] The difference in outcomes, in favor of medical treatment, persisted at 12 months but was no longer statistically significant.

Contrary to DECRA, in which decompressive craniectomy was investigated for patients with less severe intracranial hypertension that was not controlled by early interventions, the RESCUEicp investigators evaluated the effectiveness of craniectomy as a last-tier intervention for patients with TBI and refractory and sustained intracranial hypertension.[5] The RESCUEicp results were published in 2016, demonstrating significant differences in functional outcomes at 6 and 12 months. Patients who received a decompressive craniectomy had lower mortality rates, higher rates of vegetative state, and higher Extended Glasgow Outcome Scale (GOS-E) scores for vegetative state, lower severe disability (dependent), and upper severe disability (independent at home for at least 8 hours) compared with those who received medical treatment. Rates of moderate disability and good recovery were similar for both groups. The initial RESCUEicp trial results suggested that the reduced mortality rate as a result of decompressive craniectomy translates to both dependent and independent living at 6 and 12 months. Here, we report group outcomes for RESCUEicp participants at 24 months and examine the trajectory of functional outcomes from 6 to 24 months.

Key Points

Question What are the 24-month outcomes for patients with traumatic intracranial hypertension who receive a decompressive craniectomy vs standard medical treatment?

Findings In this prespecified secondary analysis of a randomized clinical trial, 408 adults received either decompressive craniectomy or standard care. The Extended Glasgow Outcome Scale was used to assess 24-month outcomes in this secondary analysis; surgical patients had sustained reduced mortality but higher rates of vegetative state, severe disability, and moderate disability at 24 months.

Meaning At 24 months, surgical patients with traumatic intracranial hypertension were more likely to improve over time compared with patients in the standard medical treatment group.

Methods

Study Design

This prespecified secondary analysis of data from the RESCUEicp randomized clinical trial was approved by the Cambridgeshire 4 Research Ethics Committee; the trial protocol is provided in Supplement 1. Ethics committee approval was also obtained from all other participating institutions outside the UK. Because this trial only enrolled patients with severe TBI, their nearest relative or designated person provided written informed consent. This study adhered to the Consolidated Standards of Reporting Trials (CONSORT) guideline.

This analysis assessed functional outcomes using GOS-E scores at 24 months. Detailed study population characteristics, recruitment, and primary results were published previously.[5] In brief, participants were recruited from 52 centers in 20 countries. Enrollment occurred between January 2004 and March 2014. Data analysis was performed between 2018 and 2021. Eligibility criteria were as follows: age 10 to 65 years, TBI confirmed with computed tomography, ongoing ICP monitoring, and increased ICP (>25 mm Hg for 1-12 hours) despite tier 1 and 2 interventions (eMethods 1 in Supplement 2). Patients with traumatic intracranial hematomas requiring immediate evacuation were included if the bone flap had been replaced (ie, they did not have a primary decompressive craniectomy). Exclusion criteria were as follows: bilateral fixed and dilated pupils, bleeding diathesis, or unsurvivable injury. All participating hospitals provide 24-hour neurosurgical services and have acute neurosciences services for patients with severe TBI. Patients were treated according to a tiered treatment protocol as described in eMethods 2 in Supplement 2. Included patients arrived needing tier 3 treatment and had elevated ICP (>25 mm Hg) for 1 to 12 hours despite tier 1 and 2 interventions. They were randomly assigned 1:1 to receive (1) a decompressive craniectomy with medical treatment (surgical group) or (2) ongoing medical treatment with the option to add barbiturate infusion (medical group).

Outcomes and Follow-up

The 24-month outcome data were part of the end points described in the trial protocol (Supplement 1) but were not included in the primary publication[5] because their collection was ongoing at the time. The 24-month outcome data were collected and analyzed with the same methodology as the 6- and 12-month outcome data.

In brief, follow-up for UK participants was performed by the trial office in Cambridge initially by mail. If no response was received, a telephone interview was conducted with patients and/or their family members to complete the GOS-E questionnaire. For non-UK sites, local members of the research team conducted the interview. Investigators blinded to treatment centrally adjudicated outcomes, as detailed by Hutchinson et al.[5]

Similar to the primary outcome measure at 6 months, outcomes in this study were assessed at 24 months with the GOS-E, a 19-item questionnaire that measures an ordinal scale of the global outcome and is commonly used as the primary outcome in trials involving neurotrauma patients. Scores range from 1 (death) to 8 (upper good recovery). The GOS-E defines 8 categories of possible outcomes based on functional independence, work, social and leisure activities, and relationships: 1 indicates death; 2, vegetative state (unable to obey commands); 3, lower severe disability (requires frequent help in daily living); 4, upper severe disability (independent at home for at least 8 hours); 5, lower moderate disability (independent at home and outside the home but with some physical or mental disability); 6, upper moderate disability (independent at home and outside the home but with some physical or mental disability, with less disruption than lower moderate disability); 7, lower good recovery (able to resume normal activities with some injury-related problems); and 8, upper good recovery (no problems).

All outcomes were reported in the intention-to-treat population, excluding patients who withdrew consent or were declared lost to follow-up. The 24-month outcomes analysis was performed on the intention-to-treat population with no imputation of missing data, in accordance with the RESCUEicp statistical analysis plan (Supplement 1) and the primary end point data published previously.[5]

Statistical Analysis

The previously published 6- and 12-month outcomes were analyzed with an unordered χ^2 test because the proportional-odds model was rejected, suggesting a GOS-E distribution difference between the 2 randomized groups.[5] Therefore, we followed the same analysis using an unordered χ^2 test to assess GOS-E differences at 24 months.

To determine GOS-E changes over time, Dunn-Bonferroni post hoc tests with Bonferroni adjustments were performed after the Friedman test to assess paired comparisons between differences between individual time points (6 vs 12, 6 vs 24, and 12 vs 24 months).

We also analyzed net change in GOS-E scores between the 6- and 24-month time points. We used the unordered χ^2 test to compare the proportions of patients with an unchanged GOS-E score and improvement or worsening by at least 1 grade between randomized groups. As a sensitivity analysis, the proportion of patients achieving upper severe disability or better on the GOS-E scale was compared between randomized groups using a χ^2 test. $P < .05$ (2-tailed) was considered significant. Statistical analysis was performed with Stata MP version 16 (StataCorp LLC).

Results

A total of 408 patients were enrolled in the RESCUEicp trial, with 206 in the surgical group and 202 in the medical group; after exclusions, there were 202 patients in the surgical group and 196 patients in the medical group (**Figure 1** and eTable 1 in Supplement 2). The mean (SD) age was 32.3 (13.2) vs 34.8 (13.7) years. In the surgical group, there were 165 men (81.7%) and 37 women (18.3%); in the medical group, there were 156 men (79.6%) and 39 women (20.0%; sex was not available for 1 patient). For the surgical vs medical groups, intention-to-treat analyses of outcomes at 6, 12, and 24 months included 389 (201 vs 188), 373 (194 vs 179), and 356 (182 vs 174) patients, respectively.

Table 1 compares population characteristics of the surgical and medical groups.[5] Outcomes classification according to full GOS-E distributions at 6, 12, and 24 months after randomization (primary and secondary analyses, modified intention-to-treat population) is detailed in **Table 2** and **Figure 2**. eTable 2 in Supplement 2 presents cross-tabulations of functional outcomes.

GOS-E Scores at 24 Months

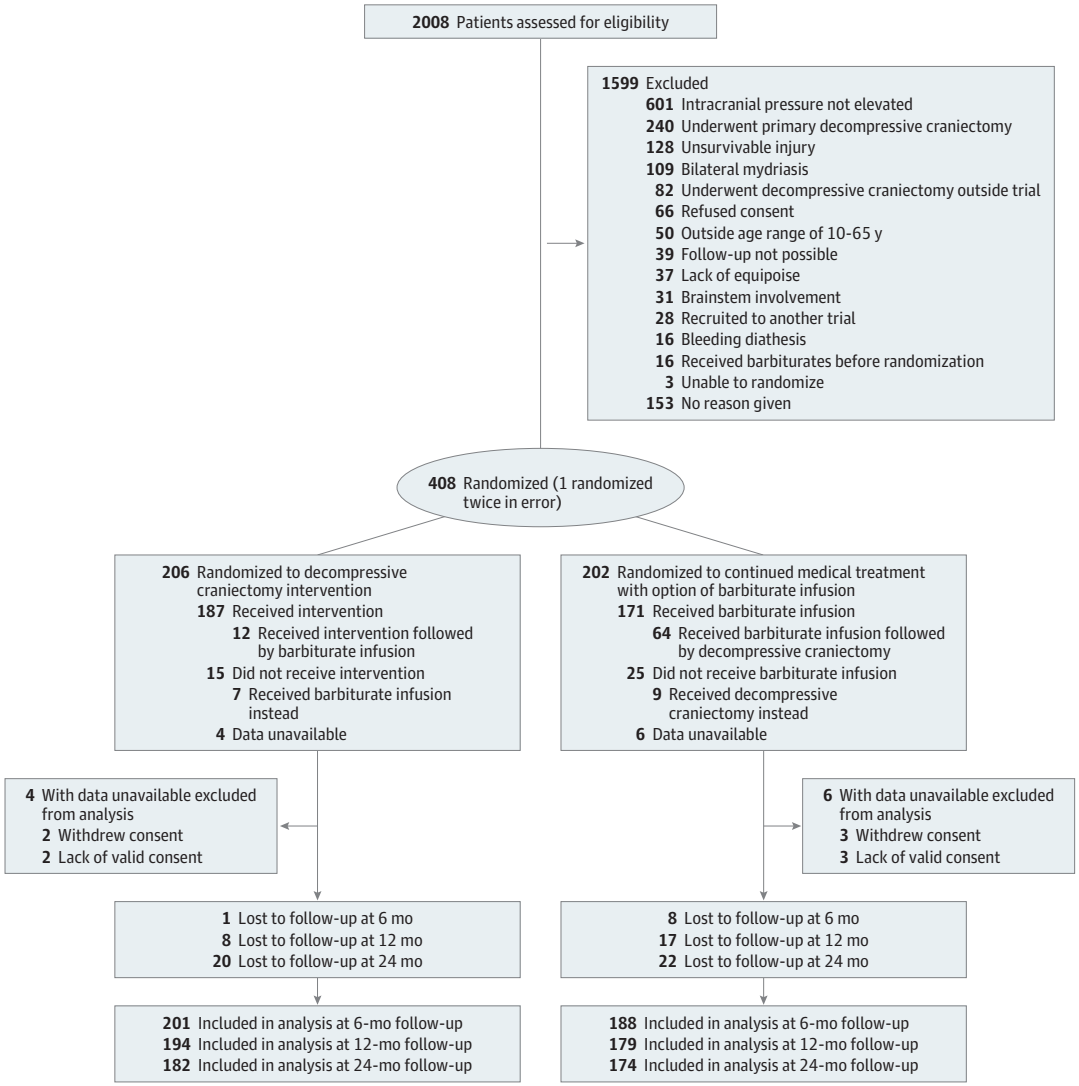
Between-group differences in GOS-E score distribution at 6 months ($\chi^2_7 = 30.69$, $P < .001$) and 12 months ($\chi^2_7 = 29.16$, $P < .001$) have been published previously (Table 2). This distribution was also sustained at 24 months ($\chi^2_7 = 24.20$, $P = .001$). For every 100 patients at 24 months who were treated with surgical rather than medical intent, there were 21 additional survivors (4 in a vegetative state, 2 with lower and 7 with upper severe disability, and 5 with lower and 3 with upper moderate disability). Rates of lower and upper good recovery were similar for the surgical and medical groups (20 [11.0%] vs 19 [10.9%]) (Table 2). In the sensitivity analysis, 82 of 182 patients (45.1%) in the surgical group and 54 of 174 (31.0%) in the medical group had a GOS-E outcome of upper severe disability or better ($\chi^2 = 7.41$, $P = .006$) (eTable 3 in Supplement 2).

Changes in GOS-E Scores Over Time

Dunn-Bonferroni post hoc tests were performed to adjust for mbxultiple testing between the various time points. Significant differences were observed between 6- and 24-month GOS-E outcomes in the surgical group ($P = .004$) (**Table 3**). No statistically significant between-group differences were found for any other time points after Bonferroni adjustments (eTable 4 in Supplement 2). Temporal changes of patient transitions across the full range of GOS-E scores for each treatment group were calculated from Table 2 and are presented in the eFigure in Supplement 2.

Significant differences in the analysis of net change in improvement or worsening by 1 GOS-E grade or more or unchanged GOS-E scores were also seen across the 2 treatment groups between 6 and 24 months ($\chi^2_2 = 13.27$, $P = .001$). A total of 55 patients (30.4%) in the surgical group achieved net improvement of 1 grade or more compared with 25 patients (14.5%) in the medical group (Table 3). The net per-

Figure 1. CONSORT Flow Diagram of RESCUEicp Participants



CONSORT indicates Consolidated Standards of Reporting Trials; RESCUEicp, Randomized Evaluation of Surgery With Craniectomy for Uncontrollable Elevation of Intracranial Pressure.

centage of worsening of both treatment groups was equal, at 8.2%. Of the study participants, 111 (61.3%) in the surgical group and 134 (77.5%) in the medical group had no change in GOS-E score.

Discussion

This randomized clinical trial found that patients with posttraumatic intractable intracranial hypertension treated with decompressive craniectomy had a sustained reduction in mortality at 24 months compared with those treated with standard medical care. However, we observed higher proportions of patients in the surgical group who were in a vegetative state or had severe or moderate disability. Additional analyses of GOS-E changes over time showed that patients in the surgical group were more likely to improve over time than patients in the medical group, as demonstrated by the paired time-point analyses. However, it is important to note that GOS-E scores for the majority of patients in both groups remained unchanged over the period from 6 to 24 months. Improvement by at least 1 grade was seen for 30.4% of the surgical group vs 14.5% of the medical group.

Previously published 6- and 12-month RESCUEicp outcome data demonstrate that mortality was 22.1% and 21.5% lower, respectively, for the surgical group than for the medical group. The proportions of patients in the surgical group who were in a vegetative state or had lower severe or upper severe disability were higher than those of the medical group; rates of moderate disability and good recovery were similar for both groups. However, at 24

Table 1. Baseline Characteristics of the Intention-to-Treat Population[a]

Characteristic	Surgical group (n = 202)	Medical group (n = 196)
Age, mean (SD), y	32.3 (13.2)	34.8 (13.7)
Sex[b]		
Men	165 (81.7)	156 (79.6)
Women	37 (18.3)	39 (20.0)
GCS motor score at first hospitalization, No./total No. (%)		
1 or 2	96/181 (53.0)	85/170 (50.0)
3-6	85/181 (47.0)	85/170 (50.0)
Pupillary abnormality	59 (29.2)	57 (29.1)
Hypotension	40 (19.8)	42 (21.4)
Hypoxemia	49 (24.3)	52 (26.5)
Extracranial injury	75 (37.1)	83 (42.3)
Injury classification based on CT imaging, No./total No. (%)		
Diffuse injury	161/198 (81.3)	141/186 (75.8)
Mass lesion	37/198 (18.7)	45/186 (24.2)

Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale.

[a] Data are presented as number (%) of patients unless indicated otherwise.

[b] Data missing for 1 patient in the medical group.

months, the rate of moderate disability was also higher in the surgical group than the medical group, with similar rates of good recovery. This observation may be because patients in the surgical group are more likely to improve over time, and as a result, shift to the better end of the GOS-E spectrum.

Compared with the DECRA trial that investigated decompressive craniectomy when early interventions failed to control intracranial hypertension, we observed substantial differences in patient outcomes in the RESCUEicp trial that examined last-tier use of decompressive craniectomy for refractory and sustained intracranial hypertension.[3] The DECRA investigators reported similar mortality rates in both groups at 6 months (19.0% and 18.0%, respectively) and 12 months (21.0% and 19.0%, respectively), whereas our findings showed a decreased mortality rate at 6 and 12 months in the surgical group with last-tier decompressive craniectomy.[4,6] Our current analysis supports these findings; we report that mortality rates at 24 months were 54.0% and 33.5% and were lower in the surgical group.

The RESCUEicp trial has other notable differences from the DECRA trial, including a larger sample size (408 vs 155), which indicates that this trial may have had greater power to detect between-group differences.[3,5] In addition, RESCUEicp had a longer follow-up time (24 vs 12 months).[6] Because of the shorter follow-up period, it is not possible to analyze the GOS-E trajectories in the DECRA trial, which is important given the findings of our study.

Much of the controversy regarding the use of decompressive craniectomy for patients with severe TBI and intracranial hypertension is possibly attributable to the paucity of good-quality, long-term outcome data from controlled studies.[7-9] Here we present outcomes at 24 months for 1 of 2 main randomized clinical trials comparing decompressive craniectomy vs medical treatment for patients with TBI. In addition, we provide data indicating that the scope of functional improvement up to 24 months after decompressive craniectomy is significant. This is an important addition to the debate and potentially raises questions regarding the assessment of the primary outcome at 6 months in similar trials.[8,10] Ongoing functional recovery past 12 months after decompressive craniectomy, as well as improved health-related quality of life up to 10 years after neurorehabilitation, has been recognized in TBI.[11,12]

In this analysis, the improvement by at least 1 point over the GOS-E scale in the surgical group from 6 to 24 months was more than double that in the medical group (30.4% vs 14.5%). This improvement could have resulted from the physiologic effects of the cranioplasty, which is usually undertaken a few months after the primary surgery, or possibly more frequent health care contact, including the provision of rehabilitation. It is possible that patients in the surgical group who remained on a surgical or hospital path as a result of cranioplasty requirements received more rehabilitation. However, the trial did not systematically collect data regarding rehabilitation, so this hypothesis cannot be corroborated. The improvement in the decompressive craniectomy group from 6 to 24 months may also indicate that cranioplasty, although it has its own attendant risks, had a positive effect on the long-term outcomes of these patients.

The current longer-term analysis reinforces our previous recommendation that clinicians should carefully counsel families of patients regarding decompressive craniectomy, taking into account the possible detrimental effects of the various treatment strategies with regard to survival and long-term outcomes.[5,13] In addition to the clinical indications, the decision to perform a decompressive craniectomy should be made by the multidisciplinary team in conjunction with the patient's closest relatives to consider the patient's wishes.

Limitations

Our study has a few limitations. More than one-third of the medical group received a decompressive craniectomy as a result of medical treatment failure, which could mitigate the observed treatment effect. Furthermore, we analyzed GOS-E scores in this trial to explore global functional outcomes after TBI; the granularity of the 8 outcome categories may not have allowed us to adequately capture functional outcome differences between the 2 treatment groups in the context of severe TBI. Because of the trial's pragmatic nature, long-term data on cranioplasty were not collected systematically. Cranioplasty could influence the trajectory of global functional outcomes because the procedure restores ICP to a normal physiologic range and has been shown to improve cerebrospinal fluid flow and cerebral metabolism.[13,14] This trial also did not evaluate the effectiveness of primary decompressive craniectomy, which is currently being investigated as part of the RESCUE-ASDH trial.

Table 2. Outcome Classification of the Intention-to-Treat Population[a]

GOS-E outcome	Surgical group (n = 202)	Medical group (n = 196)	Absolute percentage point difference (95% CI)	*P* value[b]
At 6 mo				
No. of patients	201	188	NA	<.001
Death	54 (26.9)	92 (48.9)	−22.1 (−31.5 to −12.7)	
Vegetative state	17 (8.5)	4 (2.1)	6.3 (1.9 to 10.7)	
Severe disability				
Lower	44 (21.9)	27 (14.4)	7.5 (−0.2 to 15.2)	
Upper	31 (15.4)	15 (8.0)	7.4 (1.2 to 13.6)	
Moderate disability				
Lower	20 (10.0)	19 (10.1)	−0.2 (−6.1 to 5.7)	
Upper	27 (13.4)	18 (9.6)	3.9 (−2.4 to 10.2)	
Good recovery				
Lower	5 (2.5)	6 (3.2)	−0.7 (−4.0 to 2.6)	
Upper	3 (1.5)	7 (3.7)	−2.2 (−5.4 to 1.0)	
At 12 mo				
No. of patients	194	179	NA	<.001
Death	59 (30.4)	93 (52.0)	−21.5 (−31.4 to 11.6)	
Vegetative state	12 (6.2)	3 (1.7)	4.5 (0.4 to 8.6)	
Severe disability				
Lower	35 (18.0)	25 (14.0)	4.1 (−3.4 to 11.6)	
Upper	26 (13.4)	7 (3.9)	9.5 (3.8 to 15.2)	
Moderate disability				
Lower	20 (10.3)	14 (7.8)	2.5 (−3.1 to 8.1)	
Upper	23 (11.9)	22 (12.3)	−0.4 (−7.2 to 6.4)	
Good recovery				
Lower	14 (7.2)	7 (3.9)	3.3 (−1.3 to 7.9)	
Upper	5 (2.6)	8 (4.5)	−1.9 (−5.7 to 1.9)	
At 24 mo				
No. of patients	182	174	NA	.001
Death	61 (33.5)	94 (54.0)	−20.5 (−30.8 to −10.2)	
Vegetative state	12 (6.6)	4 (2.3)	4.3 (0.0 to 8.6)	
Severe disability				
Lower	27 (14.8)	22 (12.6)	2.2 (−5.4 to 9.8)	
Upper	16 (8.8)	4 (2.3)	6.5 (1.8 to 11.2)	
Moderate disability				
Lower	19 (10.4)	10 (5.7)	4.7 (−0.9 to 10.3)	
Upper	27 (14.8)	21 (12.1)	2.8 (−4.2 to 9.8)	
Good recovery				
Lower	14 (7.7)	9 (5.2)	2.5 (−2.8 to 7.8)	
Upper	6 (3.3)	10 (5.7)	−2.5 (−6.9 to 1.9)	

Abbreviations: GOS-E, Extended Glasgow Outcomes Scale; NA, not applicable.

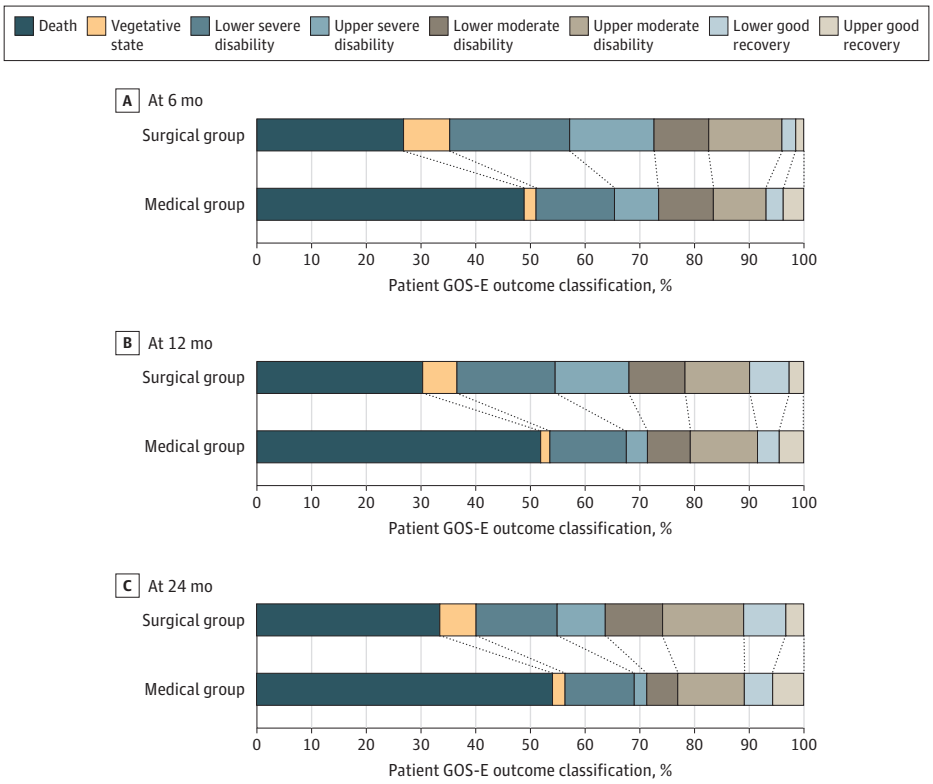
[a] Data are presented as number (%) of patients unless indicated otherwise.

[b] *P* values were calculated by the unordered χ^2 test for differences between the 2 randomized groups.

Conclusions

This secondary analysis of the RESCUEicp randomized clinical trial found that patients with intractable intracranial hypertension after TBI who received a decompressive craniectomy had a sustained reduction in mortality at 24 months compared with those who received standard medical care. For every 100 patients treated with surgical rather than medical intent, 21 additional patients survived at 24 months (4 were in a vegetative state, 2 had lower and 7 had upper severe disability, and 5 had lower and 3 had upper moderate disability). Rates of good recovery were similar in both groups. Patients in the surgical group were more likely to improve over time compared with patients in the medical group. These data support the use and potential benefit of longer-term follow-up for TBI clinical trials. There is a wide spectrum of outcomes among patients undergoing decompressive craniectomy for intractable intracranial hypertension. These findings support the notion that careful patient selection, following the principles of multidisciplinary consensus and shared decision-making with the closest relatives, is required.

Figure 2. Outcome Classifications at 6, 12, and 24 Months for Patients With Traumatic Intracranial Hypertension Treated With Surgery or Standard Medical Care



Patients with severe traumatic brain injury and sustained and refractory intracranial hypertension were randomly assigned 1:1 to decompressive craniectomy with standard care (surgical group) or to ongoing medical treatment with the option to add barbiturate infusion (medical group). Outcomes were assessed using the 8-point Extended Glasgow Outcome Scale (GOS-E), with 1 indicating death and 8 denoting upper good recovery.

Table 3. Changes in Extended Glasgow Outcomes Scale Outcome Distribution and Shift Analysis[a]

Time analysis	Surgical group	Medical group	Total
P value paired time-point comparisons of GOS-E scores[b]			
6 vs 12 mo	.07	.92	.06
6 vs 24 mo	.004	.96	.009
12 vs 24 mo	>.99	>.99	>.99
Net change in GOS-E over 24 mo, No. (%)[c]			
Worsening by ≥1 grade	15 (8.3)	14 (8.1)	29 (8.2)
Unchanged	111 (61.3)	134 (77.5)	245 (69.2)
Improvement by ≥1 grade	55 (30.4)	25 (14.5)	80 (22.6)

Abbreviation: GOS-E, Extended Glasgow Outcomes Scale.

[a] At 6, 12, and 24 months of follow-up, the analysis included 201, 194, and 182 patients in the surgical group and 188, 179, and 174 in the medical group, respectively.

[b] Dunn-Bonferroni post hoc tests with Bonferroni adjustments were carried out after the Friedman test to assess differences between time points.

[c] *P* values were calculated with the unordered χ^2 test for differences between the 2 randomized groups ($\chi^2_2 = 13.27$, $P = .001$).

ARTICLE INFORMATION

Accepted for Publication: January 28, 2022.

Published Online: June 6, 2022. doi:10.1001/jamaneurol.2022.1070

Author Affiliations: Division of Neurosurgery, Addenbrooke's Hospital, Cambridge, United Kingdom (Kolias, Adams, Timofeev, Corteen, Hossain, Pickard, Menon, Kirkpatrick); Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom (Kolias, Adams, Timofeev, Corteen, Hossain, Czosnyka, Pickard, Menon, Hutchinson); Department of Neurosurgery, Leeds General Infirmary, Leeds, United Kingdom (Timothy, Anderson); University Hospital Southampton, Southampton, United Kingdom (Bulters, Eynon); University of Birmingham, Birmingham, United Kingdom (Belli); Department of Neurosurgery, Royal London Hospital, London, United Kingdom (Wadley); Neurosurgical Trials Group, Institute of Neuroscience, Newcastle University, Newcastle, United Kingdom (Mendelow, Mitchell); Department of Neurosurgery, Imperial Neurotrauma Centre, Imperial College Academic Health Sciences Centre, St Mary's Hospital, London, United Kingdom (Wilson); Department of Neurosurgery, University Hospitals Sussex, Brighton, United Kingdom (Critchley); Department of Neurosurgery, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona, Barcelona, Spain (Sahuquillo); Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany (Unterberg); Department of Neurosurgery and Turku Brain Injury Centre, Turku University Hospital, University of Turku, Turku, Finland (Posti); Department of Biomedical Science,

Humanitas University, Milan, Italy (Servadei); Department of Neurosurgery, Istituto di Ricovero e Cura a Carattere Scientifico Humanitas Research Hospital, Milan, Italy (Servadei); Department of Neurosurgery, University of Glasgow, Glasgow, Scotland (Teasdale); Department of Community Health Sciences, Usher Institute, University of Edinburgh Medical School, Edinburgh, Scotland (Murray).

Author Contributions: Drs Kolias and Hutchinson had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Kolias and Adams served as co-first authors.
Concept and design: Kolias, Adams, Timofeev, Hossain, Czosnyka, Belli, Mendelow, Mitchell, Sahuquillo, Unterberg, Servadei, Teasdale, Pickard, Menon, Murray, Kirkpatrick, Hutchinson.
Acquisition, analysis, or interpretation of data: Kolias, Adams, Timofeev, Corteen, Hossain, Timothy, Anderson, Bulters, Eynon, Wadley, Mitchell, Wilson, Critchley, Posti, Teasdale, Menon, Murray, Hutchinson.
Drafting of the manuscript: Kolias, Adams, Hossain, Belli, Posti, Pickard, Hutchinson.
Critical revision of the manuscript for important intellectual content: Kolias, Adams, Timofeev, Corteen, Hossain, Czosnyka, Timothy, Anderson, Bulters, Belli, Eynon, Wadley, Mendelow, Mitchell, Wilson, Critchley, Sahuquillo, Unterberg, Posti, Servadei, Teasdale, Menon, Murray, Kirkpatrick, Hutchinson.
Statistical analysis: Kolias, Adams, Hossain, Mitchell, Murray, Hutchinson.
Obtained funding: Timofeev, Hossain, Bulters, Belli, Pickard, Menon, Kirkpatrick, Hutchinson.
Administrative, technical, or material support: Adams, Timofeev, Corteen, Hossain, Mitchell, Critchley, Sahuquillo, Hutchinson.
Supervision: Kolias, Czosnyka, Timothy, Mendelow, Mitchell, Critchley, Sahuquillo, Unterberg, Servadei, Kirkpatrick, Hutchinson.

Conflict of Interest Disclosures: Dr Kolias reported receiving grants from the Medical Research Council during the conduct of the study. Dr Hossain reported receiving the Integra EANS grant from the European Association of Neurosurgical Societies and a research grant from the Finnish Medical Foundation during the conduct of the study. Dr Belli reported receiving grants from the UK National Institute for Health and Care Research (NIHR) during the conduct of the study. Dr Mendelow reported serving as the director of Newcastle Neurosurgery Foundation Ltd outside the submitted work. Dr Posti reported receiving grants from the Academy of Finland and the Maire Taponen Foundation during the conduct of the study. Dr Pickard reported receiving grants from the University of Cambridge during the conduct of the study. Dr Menon reported receiving grants from NIHR during the conduct of the study as well as grants from PressuraNeuro and GlaxoSmithKline and personal fees from Lantmannen AB, NeuroTrauma Sciences, Calico, and Integra Neurosciences (for educational activities) outside the submitted work. No other disclosures were reported.

Funding/Support: This work was supported by grant 09/800/16 from the Medical Research Council (MRC) and managed by the UK National Institute for Health and Care Research (NIHR) on behalf of the MRC-NIHR partnership. This work was also supported by the NIHR Cambridge Biomedical Research Centre, the Academy of Medical Sciences and Health Foundation (Senior Fellowship to Dr Hutchinson), and the Evelyn Trust.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The RESCUEicp Trial Collaborators are listed in Supplement 3.

Data Sharing Statement: See Supplement 4.

Additional Contributions: We thank Max Pitches for administrative support throughout the trial. There was no financial compensation for this contribution.

REFERENCES

1. Kolias AG, Kirkpatrick PJ, Hutchinson PJ. Decompressive craniectomy: past, present and future. *Nat Rev Neurol*. 2013;9(7):405-415. doi:10.1038/nrneurol.2013.106

2. Kolias AG, Viaroli E, Rubiano AM, et al. The current status of decompressive craniectomy in traumatic brain injury. *Curr Trauma Rep*. 2018;4(4):326-332. doi:10.1007/s40719-018-0147-x

3. Cooper DJ, Rosenfeld JV, Murray L, et al; DECRA Trial Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493-1502. doi:10.1056/NEJMoa1102077

4. Sahuquillo J, Martínez-Ricarte F, Poca MA. Decompressive craniectomy in traumatic brain injury after the DECRA trial. Where do we stand? *Curr Opin Crit Care*. 2013;19(2):101-106. doi:10.1097/MCC.0b013e32835eba1a

5. Hutchinson PJ, Kolias AG, Timofeev IS, et al; RESCUEicp Trial Collaborators. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med*. 2016;375(12):1119-1130. doi:10.1056/NEJMoa1605215

6. Cooper DJ, Rosenfeld JV, Murray L, et al; DECRA Trial Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. Patient outcomes at twelve months after early decompressive craniectomy for diffuse traumatic brain injury in the randomized DECRA clinical trial. *J Neurotrauma*. 2020;37(5):810-816. doi:10.1089/neu.2019.6869

7. Honeybul S, Ho KM, Gillett GR. Long-term outcome following decompressive craniectomy: an inconvenient truth? *Curr Opin Crit Care*. 2018;24(2):97-104. doi:10.1097/MCC.0000000000000481

8. Kwan K, Schneider J, Ullman JS. Decompressive craniectomy: long term outcome and ethical considerations. *Front Neurol*. 2019;10:876.

9. Rubiano AM, Carney N, Khan AA, Ammirati M. The role of decompressive craniectomy in the context of severe traumatic brain injury: summary of results and analysis of the confidence level of conclusions from systematic reviews and meta-analyses. *Front Neurol*. 2019;10:1063. doi:10.3389/fneur.2019.01063

10. Honeybul S, Ho KM, Lind CRP, Gillett GR. Observed versus predicted outcome for decompressive craniectomy: a population-based study. *J Neurotrauma*. 2010;27(7):1225-1232. doi:10.1089/neu.2010.1316

11. Ho KM, Honeybul S, Litton E. Delayed neurological recovery after decompressive craniectomy for severe nonpenetrating traumatic brain injury. *Crit Care Med*. 2011;39(11):2495-2500. doi:10.1097/CCM.0b013e318225764e

12. Rauen K, Reichelt L, Probst P, et al. Decompressive craniectomy is associated with good quality of life up to 10 years after rehabilitation from traumatic brain injury. *Crit Care Med*. 2020;48(8):1157-1164. doi:10.1097/CCM.0000000000004387

13. Hutchinson PJ, Kolias AG, Tajsic T, et al. Consensus statement from the International Consensus Meeting on the Role of Decompressive Craniectomy in the Management of Traumatic Brain Injury. *Acta Neurochir (Wien)*. 2019;161(7):1261-1274. doi:10.1007/s00701-019-03936-y

14. Honeybul S, Janzen C, Kruger K, Ho KM. The impact of cranioplasty on neurological function. *Br J Neurosurg*. 2013;27(5):636-641. doi:10.3109/02688697.2013.817532