Significance of intracranial pressure and cerebral perfusion pressure in severe pediatric traumatic brain injury

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Key words: *cerebral perfusion pressure; intracranial pressure; decompressive craniotomy; severe head injury.*

Summary. *The aim of the study was to evaluate outcome of children after severe traumatic brain injury treated according to intracranial pressure (ICP)-targeted protocol, to define threshold values of peak ICP and minimal cerebral perfusion pressure (CPP) for decompressive osteoplastic craniotomy, and to determine the relationship between ICP, CPP and long-term outcome in these children.*

All children admitted to Pediatric Intensive Care Unit of Kaunas University of Medicine Hospital after severe head injury from January 2004 to June 2006 and treated according to ICP-targeted protocol for the management of severe head trauma were prospectively included in the study. Raised ICP was defined as a level higher than 20 mmHg. Minimal CPP was considered to be at a level of 40 mmHg. Outcome was defined using Glasgow Outcome Scale (GOS) at discharge from the hospital and after 6 months.

Forty-eight patients (32 boys and 16 girls) were included into the study. Favorable outcome (GOS score of 4 and 5) after 6 months was achieved in 43 (89.6%) cases. Mean peak ICP was 24.2±7.2 mmHg and mean minimal CPP – 53.1±14.7 mmHg. Decompressive craniotomy was performed in 13 cases. Threshold values of peak ICP and minimal CPP for decompressive craniotomy were 22.5 mmHg (area under the curve, 0.880) and 46.5 mmHg (area under the curve, 0.898), respectively. The differences in peak ICP and minimal CPP in groups of favorable and unfavorable outcomes were not statistically significant.

Treating children after severe traumatic brain injury according to the ICP-targeted protocol for the management of severe pediatric traumatic brain injury resulted in a favorable long-term outcome.

Introduction

Traumatic brain injury (TBI) causes significant morbidity and mortality in children (1). In contrast to adult practice, severe traumatic brain injury is more commonly isolated injury in children (2). Children who sustain traumatic brain injuries are more often injured severely in comparison to children who sustain other types of injuries (3). In the last decade, there has been significant progress in the area of pediatric neurotrauma management. Elucidation of important pathological mechanisms leading to secondary brain lesions, a better understanding of the consequences of therapeutic agents for brain physiology and the development of multimodal monitoring have led to changes in standard practice (4). In patients with severe TBI, mortality is usually caused by an untreatable increase in intracranial pressure (ICP) (5). Children are more likely to suffer increased intracranial pressure and diffuse cerebral injury than adults who tend to develop focal intracranial lesions. Management of severe TBI in the intensive care unit (ICU) is largely focused on the management of raised intracranial pressure and preservation of cerebral perfusion (1, 6–8). However, there is a lack of data on optimal cerebral perfusion pressure (CPP) and ICP targets for pediatric TBI (9).

Methods and materials

The aim of the study was to evaluate outcome of children after severe traumatic brain injury treated according to ICP-targeted protocol of the management of severe pediatric TBI, to define threshold values of

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peak ICP and minimal CPP for decompressive craniotomy, and to determine the relationship between ICP, CPP and long-term outcome in those children.

The study was performed with the permission of the Ethical Committee of Kaunas University of Medicine (No. BE-2-46; 09-21-2005).

All children admitted to Pediatric Intensive Care Unit (PICU) of Kaunas University of Medicine Hospital (KUMH) after severe head injury from January 2004 to June 2006 and treated according to ICP-targeted protocol of severe head trauma management were prospectively included in the study. The severity of head injury was categorized according to postresuscitation Glasgow Coma Scale (GCS) 8 or less (10). GCS core was determined during first hour after admission to PICU of KUMH or other hospital. General management included intubation, ventilation, oxygenation, head elevation, fluid resuscitation with normal saline and fluid restriction up to 75% of physiological fluid requirement afterwards, sedation, analgesia, muscle relaxation, normoventilation, and normothermia. Vasoactive agents (dopamine and norepinephrine) were used if needed in order to maintain optimal mean arterial pressure (MAP). MAP was determined by continuous invasive monitoring.

ICP was monitored with an intraparenchymal sensor (Codman MicroSensor). No complications or side effects caused by intraparenchymal sensor placement were observed. Raised ICP was defined as a level higher than 20 mmHg on more than 1 hourly recording at any point during ICU stay. CPP was defined as CPP=MAP–ICP. Minimal CPP was considered to be at a level of 40 mmHg. This threshold is consistent with guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents (11). Strategy of raised ICP management included mannitol, hypertonic saline (maintaining serum sodium level not lower than 140 mmol/L), mild hyperventilation and barbiturates and decompressive craniotomy for refractory intracranial hypertension. Decompressive surgery for cerebral edema was performed in the absence of mass lesions, with the bone flap left to be replaced at an elective date. Outcome was measured using Glasgow Outcome Scale (GOS) (12, 13) on discharge from the hospital and after 6 months (10). Patients were divided into groups of "favorable" and "unfavorable" outcome. Patients with moderate disability and good recovery were regarded as having "favorable" outcome, while severe disability, vegetative survival, or death were considered to be an "unfavorable" outcome (13). The method of follow-up used was a telephone interview.

Forty-eight patients (32 boys and 16 girls) were included into the study. The mean age was 10.6±5.2 years, ranging from 2.4 months to 18 years. Nine patients were admitted directly to KUMH; 39 were transported from a regional hospital by transportation team from KUMH. Mean arrival time at the hospital was 3.5±3.6 for those who were admitted straightly to KUMH and 8.3±8.1 for those transported from regional hospitals.

Statistical analysis of the data was performed by using SPSS 12 software package. Data are expressed as mean ± standard deviation (SD) or percentage as appropriate. After testing for normality, Pearson correlation coefficient was used to define correlation between variables; Student t and Mann–Whitney tests were used for comparison of means. A p less than 0.05 was considered statistically significant. Receiver operating characteristic curves (ROC curves) (14) were drawn out to determine the threshold values of ICP and CPP for performing decompressive craniotomy.

Results

The survival rate was 97.9%. Only one patient (2.1%) died on the first day of ICU stay. Detailed distribution of GOS after 6 months is shown in Fig. 1. Favorable outcome (GOS score of 4 and 5) after 6 months was achieved in 43 (89.6%) cases. The mean ICP monitoring time was 3.5±1.7 days (range, 1 to 7 days). The mean peak ICP was 24.2±7.2 mmHg and mean minimal CPP – 53.1±14.7 mmHg. A moderate negative correlation was determined between these two variables (Fig. 2). A moderate positive correlation was determined between ICP and ventilation time ($r=0.4$, $P<0.05$), and a weak negative correlation – between CPP and ICU stay ($r=–0.3$, $P<0.05$). Decompressive craniotomy was performed in 13 (27.1%) cases. In all cases, it was bifrontotemporoparietal. The mean peak ICP was significantly higher in patients who underwent craniotomy (30.9±6.7 mmHg *vs.* 21.8±5.6 mmHg), and the mean minimal CPP in those patients was significantly lower (39.5±8.2 mmHg *vs.* 58.1±12.8 mmHg, $P<0.05$). Threshold value of peak ICP for decompressive craniotomy was 22.5 mmHg (area under the curve, 0.880) (Fig. 3). Threshold value of minimal CPP for decompressive craniotomy was 46.5 mmHg (area under the curve, 0.898) (Fig. 4). Changes in outcomes at discharge and after 6 months were statistically significant (Table). The differences in peak ICP and minimal CPP in groups of favorable and unfavorable outcomes were not statistically significant: mean peak of ICP 22.2±4.5 mmHg and 24.6± 7.5 mmHg ($P>0.05$), minimal mean of CPP 54.8±14.8 mmHg and 44.4±9.2 mmHg ($P>0.05$). The difference

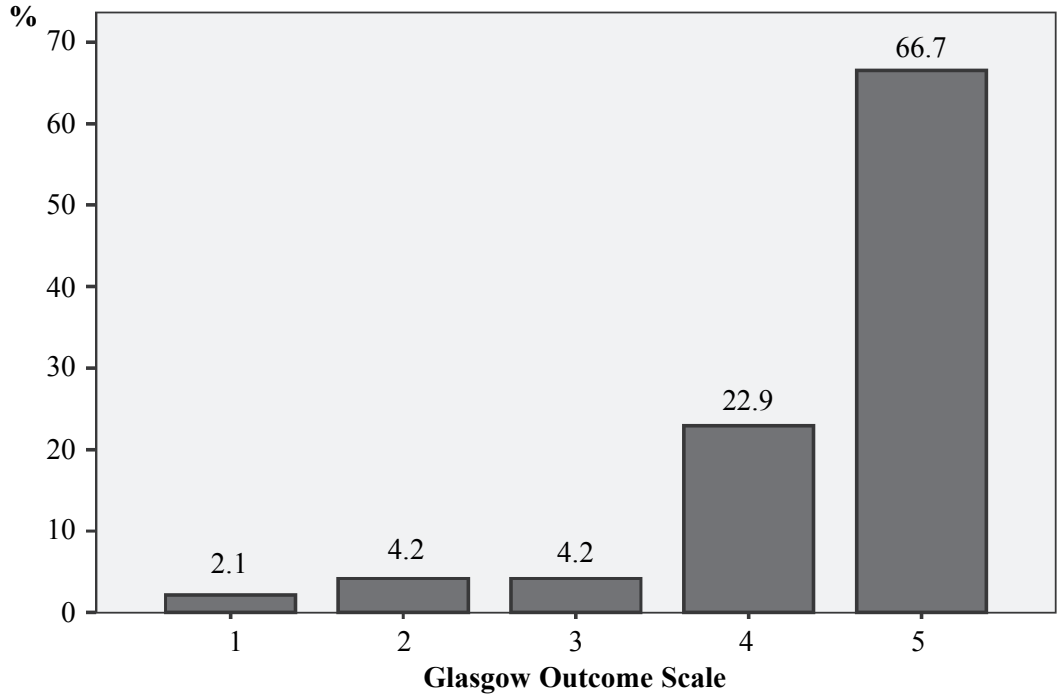

Fig. 1. **Outcome according to Glasgow Outcome Scale, expressed in percentage, at 6 months after injury**

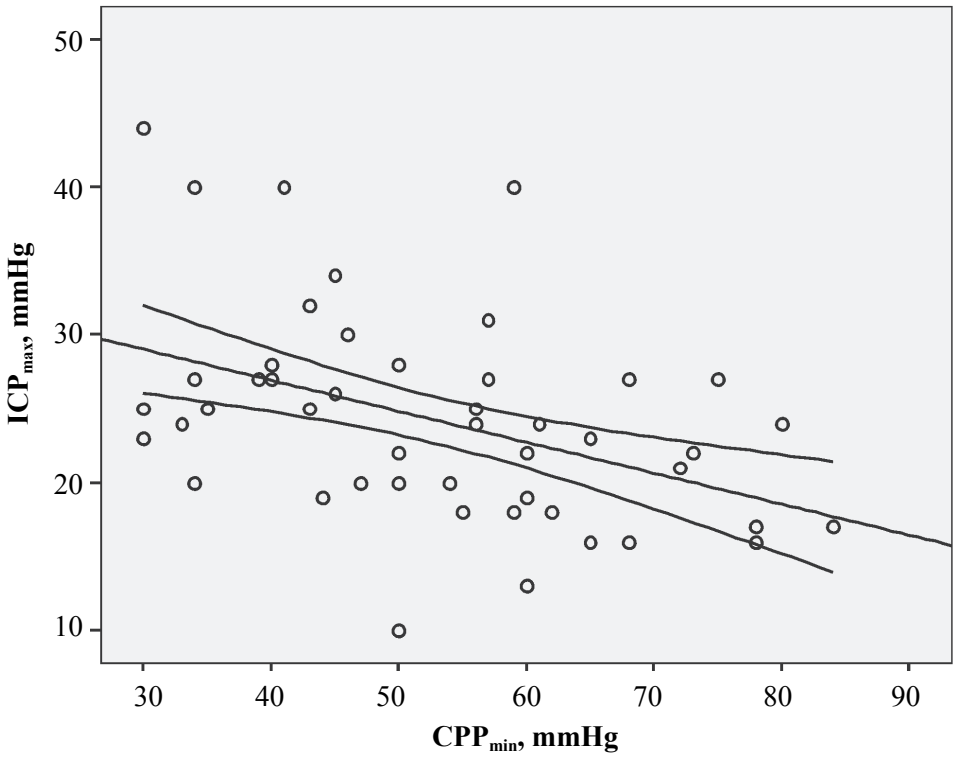

Fig. 2. **Correlation between mean ICP$_{max}$ and CPP$_{min}$**
Pearson correlation coefficient r=–0.4 (P=0.002).

in outcomes between patients with performed and not performed decompressive craniotomy was not significant (P>0.05).

Discussion

The need to prevent raised ICP is recognized as central to current intensive care practice (15). In adults,

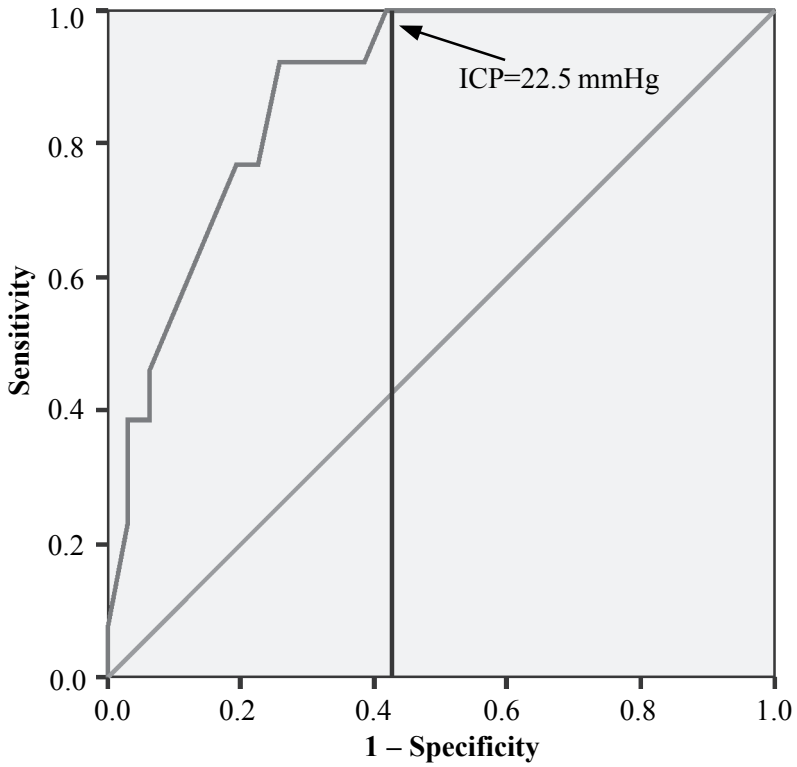

Fig. 3. **Receiver operating characteristic (ROC) curve of intracranial pressure (ICP) for performing decompressive craniotomy**
Area under the curve, 0.880; sensitivity, 1.0; specificity, 0.581; threshold value of ICP for performing decompressive craniectomy, 22.5 mmHg.

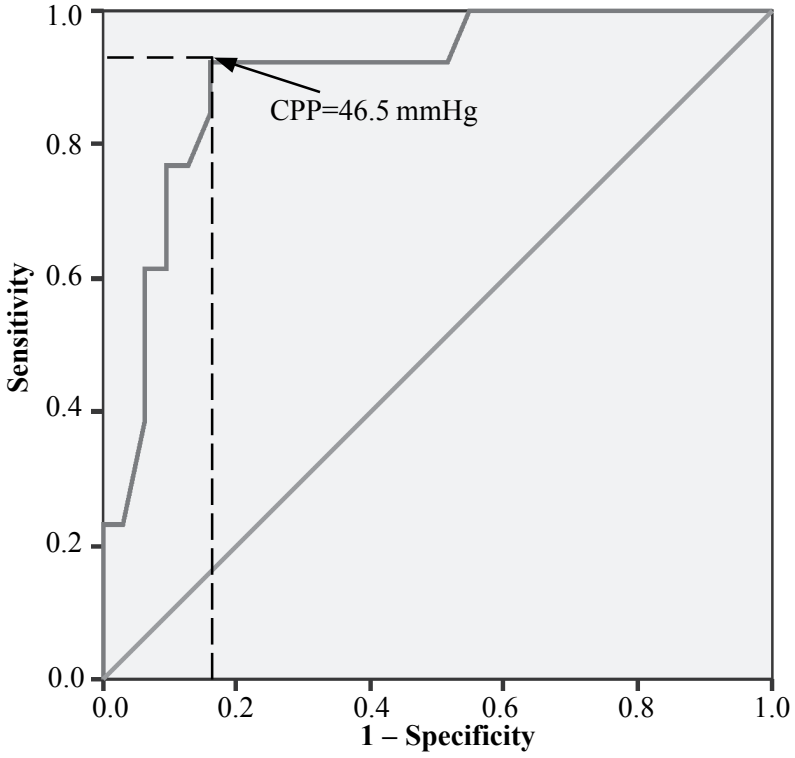

Fig. 4. **Receiver operating characteristic (ROC) curve of cerebral perfusion pressure (CPP) for performing decompressive craniotomy**
Area under the curve, 0.898; sensitivity, 0.923; specificity, 0.839; threshold value of CPP for performing decompressive craniectomy, 46.5 mmHg.

Table. **Changes in outcomes assessed using Glasgow Outcome Scale at discharge and after 6 months (P<0.05)**

Outcome at discharge	Outcome after 6 months		
	unfavorable	favorable	total
Unfavorable	5	14	19
Favorable	0	29	29
Total	5	43	48

the goal of ICP management is to maintain levels below 20 mmHg, and CPP should be maintained above 70 mmHg, to avert ischemia and below 110 mmHg to avoid breakthrough hyperperfusion (16). Currently, however, there is no consensus on the level at which CPP should be maintained to optimize outcome in children with head injury (17). Based on normative data, lower values for acceptable thresholds are likely in infants and young children, versus older children and adults (17). The guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents (11) suggest that a CPP greater than 40 mmHg should be maintained. This value is based on the work of Downard *et al.* who state that low mean CPP is lethal, and in children with survivable brain injury (mean CPP>40 mmHg), CPP did not stratify patients for risk of adverse outcome (18). Other study by Hackbar *et al.* concludes that the ability to maintain a cerebral perfusion pressure of > or = 50 mmHg was the single most important predictor of traumatic brain injury survival (19). Chambers *et al.* in the study of 235 children suggest minimum CPP values of 53, 63, and 66 mmHg for children between ages of 2 and 6, 7 and 10, and 11 and 16 years (20). A year later the same authors in a prospective observational study of 99 head-injured children defined age-related threshold levels of CPP: 2–6 years – 48 mmHg; 7–10 years – 54 mmHg; 11–16 years – 58 mmHg (21). In a 9-year retrospective review of 156 pediatric patients after severe TBI performed by Catala-Temprano *et al.*, patients with initial CPP between 40 and 70 mmHg were found to have better neurological prognosis than those with CPPs either higher or lower than that range (22). In our study mean peak ICP was higher than recommended in most studies and guidelines (1, 11, 20, 21), but CPP was maintained rather high (53.1 mmHg), and there were no differences in ICP and CPP between groups of favorable and unfavorable outcomes.

Decompression of the brain has been in existence for hundreds years, initially in terms of trepanation by the Ancient Greeks (23). While pediatric craniotomy has often been viewed as a last resource in the pediatric population, it can be an effective method of controlling ICP and providing reasonable quality of life postoperatively (24). The use of decompressive craniotomy may be of greater benefit to children than to adult patients, because the proportional incidence of diffuse injury in pediatric TBI is higher (25), and surgical decompression provides rapid relief of increased intracranial pressure and is alternative to maximal medical therapy for these individuals (26). Simma *et al.* observed a significant decrease of ICP after decompressive craniotomy from mean of 51±5 to 8±6 mmHg (27). Reviewing literature considering decompressive craniotomy in children, there is a variety of articles, ranging from case reports (25, 28–30) to retrospective reviews (31) and pilot studies (32). The studies that describe the potential benefits of performing decompressive craniotomy in the pediatric population after trauma are limited by a small sample size, short follow-up, and variable criteria used for when to operate. Some of the studies have rather unfavorable outcomes (31). Only one randomized trial was performed by Taylor *et al*. The study concluded that when children with traumatic brain injury and sustained intracranial hypertension are treated with a combination of very early decompressive craniotomy and conventional medical management, it is more likely that ICP will be reduced, fewer episodes of intracranial hypertension will occur, and functional outcome and quality of life may be better than in children treated with medical management alone (33). Although initially regarded as a second tier approach to refractory intracranial hypertension, early decompressive craniotomy seems to have a growing role in TBI management. This procedure is of relatively low risk. As such, it is useful in two situations: when ICP is becoming increasingly difficult to control (*e.g.*, anticipation of subsequent refractory intracranial hypertension) and when ICP management collides with the treatment of extracranial abnormalities (34).

Despite significantly higher ICP and lower CPP in the group of patients who underwent craniotomy, there were no differences in long-term outcomes.

Threshold value of minimal CPP for decompressive craniotomy in our study was 46.5 mmHg. Though it is relatively lower than recommended in many studies (19–21), treating patients according to the ICP-targeted protocol for the management of severe pediatric TBI and thus combining medical management with decompressive craniotomy helped to reach favorable outcome (GOS score of 4 and 5) after 6 months in 43 (89.6%) cases. Targeted therapy supports a physiology-based approach. Instead of simply targeting the ICP level, one now should concentrate on such issues as blood flow, metabolism, compliance, and so forth as underlying processes that may need concomitant manipulation. Such an approach should facilitate effective treatment while avoiding overtreatment and unnecessary procedures. Under such a system, such values as ICP and CPP will most likely evolve into treatment variables rather than "magic numbers"(34).

Conclusions

1. Treating children after severe traumatic brain injury according to the intracranial pressure-targeted protocol for the management of severe pediatric traumatic brain injury resulted in an 89.6% favorable long-term outcome.

2. Threshold values of peak intracranial pressure and minimal cerebral perfusion pressure for decompressive craniotomy were 22.5 mmHg and 46.5 mmHg, respectively.

3. The differences in peak intracranial pressure and minimal cerebral perfusion pressure in groups of favorable and unfavorable outcomes were not statistically significant.

Vidinio kaukolės slėgio ir smegenų perfuzinio slėgio svarba gydant sunkią galvos smegenų traumą vaikams

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Raktažodžiai: smegenų perfuzinis slėgis, vidinis kaukolės slėgis, dekompresinė kraniotomija, sunki galvos trauma.

Santrauka. *Tyrimo tikslas.* Įvertinti gydymo baigtis vaikams, kurie po sunkios galvos smegenų traumos buvo gydyti pagal protokolą, pagrįstą vidinio kaukolės slėgio mažinimu, nustatyti kritines aukščiausio vidinio kaukolės slėgio ir žemiausio smegenų perfuzinio slėgio ribas, prieš atliekant dekompresinę osteoplastinę kraniotomiją, ir nustatyti ryšį tarp vidinio kaukolės slėgio bei smegenų perfuzinio slėgio ir baigčių.

Prospektyviai tirti vaikai, patyrę sunkią galvos smegenų traumą ir gydyti pagal protokolą, pagrįstą vidinio kaukolės slėgio mažinimu Kauno medicinos universiteto klinikų Vaikų intensyviosios terapijos skyriuje nuo 2004 m. sausio iki 2006 m. birželio mėn. Padidėjęs vidinis kaukolės slėgis – tai slėgis didesnis nei 20 mmHg. Minimali smegenų perfuzinio slėgio riba – 40 mmHg. Baigtys vertintos pagal GOS (Glazgo baigčių skalę, angl. *Glasgow Outcome Scale*) išrašant pacientą iš ligoninės ir po šešių mėnesių.

Tyrime dalyvavo 48 vaikai (32 berniukai ir 16 mergaičių). Gera baigtis (GOS 4 ir 5) po šešių mėnesių konstatuota 43 (89,6 proc.) vaikams. Aukščiausio vidinio kaukolės slėgio vidurkis±SD – 24,2±7,2, žemiausio smegenų perfuzinio slėgio – 53,1±14,7. Dekompresinė kraniotomija atlikta 13 vaikų. Kritinės aukščiausio vidinio kaukolės slėgio ir smegenų perfuzinio slėgio ribos dekompresinei kraniotomijai atlikti buvo 22,5 mmHg (plotas po kreive =0,880) ir 46,5 mmHg (plotas po kreive =0,898). Gerų ir blogų baigčių grupėse skirtumai tarp aukščiausio vidinio kaukolės slėgio ir minimalaus smegenų perfuzinio slėgio statistiškai nereikšmingi.

Vaikų, po sunkios galvos traumos, gydytų pagal vidinio kaukolės slėgio mažinimo protokolą, ligos baigtys yra geros.

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