Preoperative identification of neurosurgery patients with a high risk of in-hospital complications: a prospective cohort of 418 consecutive elective craniotomy patients

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OBJECT Patients undergoing craniotomy are routinely assessed preoperatively, yet the role of these assessments in predicting outcome is poorly studied. This study aimed to identify preoperative factors predicting in-hospital outcome after cranial neurosurgery.

METHODS The study cohort consisted of 418 consecutive adults undergoing elective craniotomy for any intracranial lesion. Apart from the age criteria (≥ 18 years), almost all patients were considered eligible for the study to increase external validity of the results. The studied preoperative assessments included various patient-related data, routine blood tests, American Society of Anesthesiologists (ASA) Physical Status Classification system, and a local modification of the ASA classification (Helsinki ASA classification). Adverse outcomes were in-hospital mortality, in-hospital systemic or infectious complications, and in-hospital CNS deficits. Resource use was defined as length of stay (LOS) in the intensive care unit and overall LOS in the hospital.

RESULTS The in-hospital mortality rate was 1.0%. In-hospital systemic or infectious complications and permanent or transient CNS deficits occurred in 6.7% and 11.2% of the patients, respectively. Advanced age (≥ 60 –65 years), elevated C-reactive protein level (> 3 mg/L), and high Helsinki ASA score (Class 4) were associated with in-hospital systemic and infectious complications, and a combination of these could identify one-fourth of the patients with postoperative complications. Moreover, this combination of preoperative assessment parameters was significantly associated with increased resource use.

CONCLUSIONS In this first prospective and unselected cohort study of outcome after elective craniotomy, simple preoperative assessments identified patients with a high risk of in-hospital systemic or infectious complications as well as extended resource use. Presented risk assessment methods may be widely applicable, also in low-volume centers, as they are based on composite predictors and outcome events.

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KEY WORDS craniotomy; elective; outcome; preoperative assessment

DUE to the increasing awareness and demand for improving the value of care—that is, the patient's outcome relative to the cost of care—the frequency and predictors of complications have become of significant interest to health care providers. The American Society of Anesthesiologists (ASA) Physical Status Classification system is the most well-known preoperative risk estimate used for surgical patients worldwide,^{3,4} but more

customized risk prediction scores have emerged in a few subspecialties of major surgery, including cardiac surgery.⁷ The risk predicting the value of the ASA class has not been confirmed in cranial neurosurgery, and no customized risk scores exist.⁹ A recent large registry-based study with more than 38,000 neurosurgical patients (10,041 cranial neurosurgery patients) examined the frequency and predictors of complications in the United States from 2006

ABBREVIATIONS ASA = American Society of Anesthesiologists; BMI = body mass index; CRP = C-reactive protein; ICU = intensive care unit; LOS = length of stay; PT = prothrombin time.

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to 2011.¹⁰ This retrospective study could not assess the role of routine preoperative blood tests, ASA class, or any other preoperative risk score in outcome prediction. Furthermore, the reliability of predicting outcomes by using registry-based data has been questioned by others⁵ and even by the authors themselves,¹⁰ specifically since in many large registries detailed preoperative patient data are lacking. Another major problem is that the type and rate of complications in neurosurgery are variable but limited. Thus, single predictors cannot reliably predict single complications.⁵

A traditional view suggests that in cranial neurosurgery, primarily the location and nature of the lesion together with the surgeon's expertise determine the risk of adverse outcome. However, if adverse outcome in cranial neurosurgery is seen more as a multifactorial entity, objective and patient-related parameters of physical status can have an effect on the short-term outcome. Evidence supporting the use of any preoperative risk assessment scores for predicting outcome in a consecutive series of elective craniotomy patients is lacking.⁹ In an attempt to bridge this gap in knowledge, we aimed to define a composite of prospectively recorded factors, all routinely recorded in preoperative anesthesia assessments, which could be used in predicting short-term outcome and resource use after elective cranial neurosurgery.

Methods

Study Setting

This study was reviewed and approved by the ethics committee of the Hospital District of Helsinki and Uusimaa. All subjects signed a written informed consent.

We collected a consecutive series of patients undergoing elective craniotomy in the Department of Neurosurgery, Helsinki University Central Hospital, between December 7, 2011, and December 31, 2012. Helsinki University Central Hospital is a public high-volume hospital complex with a neurosurgical department with more than 3200 operations annually. Finland has a publicly funded health care system, which offers social and health care for all citizens (http://www.stm.fi/en/social_and_health_services/health_services). In general, all craniotomies are performed in one of the 5 public university hospitals in Finland. Helsinki University Central Hospital is the largest of these 5 university hospitals, and its catchment area has nearly 2 million people.

Study Population

Adult (≥ 18 years) patients scheduled for elective cranial operations under general anesthesia were eligible to participate in the study. Elective craniotomy was defined as a craniotomy performed no earlier than 7 days after the treatment decision. Exclusion criteria included 1) a lack of fluency in Finnish or Swedish (the official languages in Finland), 2) age younger than 18 years, 3) epilepsy as an indication for craniotomy (implantations of electrode grids for electrocorticographic recordings and subsequent resections of epileptogenic zones), or 4) inability to communicate because of severe underlying illness or advanced cognitive dysfunction. Patients with multiple elective cra-

niotomies during the study period were enrolled only once at the time of the first craniotomy.

Data Collection

Preoperative radiological imaging studies as well as consultations with anesthesiologists and neurosurgeons adhered to the department's standard practice. Anesthesia, surgery, and postoperative care in the neurosurgical intensive care unit (ICU) also followed the normal routines and protocols of the department. In brief, the overall treatment was unaffected by this study. Since most of the medical data during the hospital stay are routinely recorded into electronic hospital databases and patient records, we retrieved all relevant and additional patient data from these sources when necessary.

Preoperative Patient-Related Data

Anesthesiologists or neurosurgical nurses recorded data on age, sex, weight, height, body mass index (BMI), systolic blood pressure, diastolic blood pressure, and heart rate 1–30 days before the operation at the neurosurgical ward or at a preoperative outpatient clinic.

Preoperative ASA Classes

During the preoperative assessment, one of the anesthesiologist authors determined the ASA class according to the original ASA criteria and also according to a local modification of the ASA (Helsinki ASA) criteria (Table 1). The Helsinki ASA classification was implemented into clinical use at our institution in the 1990s. The neuroanesthesiologists considered the modification essential due to the clinic's patient profile with emphasis on intracranial vascular surgery. The Helsinki ASA classification system has not been validated and was not modified for the purposes of this study.

Preoperative Blood Tests

Preoperative blood tests followed the normal routines and protocols of the unit and included hemoglobin, platelets, creatinine, blood glucose (not fasting), C-reactive protein (CRP), sodium, potassium, and prothrombin time (PT). These blood tests took place within 1 week before the clinical preoperative assessment.

Follow-Up Data

Before discharge from the study hospital, one of the authors recorded the in-hospital mortality, systemic and infectious complications, and CNS deficits.

End Points

Adverse outcomes and resource use were chosen as end points. Adverse outcomes included in-hospital mortality, in-hospital systemic and infectious complications (deep vein thrombosis, pulmonary embolism, acute myocardial infarction, new ventricular arrhythmias, cardiogenic shock, cardiac arrest, pneumonia, meningitis, sepsis), and in-hospital CNS deficits (a new or worsened hemiparesis, stroke [clinical and/or radiological]; transient or permanent). Resource use was defined as length of stay (LOS) in the ICU and hospital.

TABLE 1. American Society of Anesthesiologists Physical Status Classification and its modifications

ASA Class	ASA Classification System			
	1941*	1962/1963†	Today‡	Helsinki ASA
1	"No organic pathology or patients in whom the pathological process is localized and does not cause any systemic disturbance or abnormality."	"A normal healthy patient."	"A normal healthy patient"	A previously healthy patient, age <65 years
2	"A moderate but definite systemic disturbance, caused either by the condition that is to be treated by surgical intervention or which is caused by other existing pathological process, forms this group."	"A patient with a mild systemic disease."	"A patient with mild systemic disease"	A previously healthy, age ≥65 years A patient with mild systemic disease
3	"Severe systemic disturbance from any cause or causes. It is not possible to state an absolute measure of severity, as this is a matter of clinical judgment."	"A patient with a severe systemic disease that limits activity, but is not incapacitating."	"A patient with severe systemic disease"	A patient with severe systemic disease A previously healthy patient <65 years, who has a small unruptured intracranial aneurysm or a small brain tumor with no symptoms/mild symptoms
4	"Extreme systemic disorders which have already become an eminent threat to life regardless of the type of treatment. Because of their duration or nature there has already been damage to the organism that is irreversible. This class is intended to include only patients that are in an extremely poor physical state. There may not be much occasion to use this classification, but it should serve a purpose in separating the patient in very poor condition from others."	"A patient with an incapacitating systemic disease that is a constant threat to life."	"A patient with severe systemic disease that is a constant threat to life"	A patient with unbalanced systemic disease A previously healthy patient with a clearly symptomatic intracranial aneurysm or brain tumor
5	"Emergencies that would otherwise be graded in Class 1 or Class 2."	"A moribund patient not expected to survive 24 hours with or without operation."	"A moribund patient who is not expected to survive without the operation"	A moribund patient who is not expected to survive without the operation
6	"Emergencies that would otherwise be graded in Class 3 or Class 4"		"A declared brain-dead patient whose organs are being removed for donor purposes"	
E		"In the event of emergency procedure, precede the number with an E."		

* From Saklad: *Anesthesiology* 2:281–284, 1941.

† From American Society of Anesthesiologists: *Anesthesiology* 24:111, 1963.

‡ From American Society of Anesthesiologists website (<http://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>).

Statistical Analyses

Given the principal idea of defining a new combination of outcome predictors instead of single independent outcome predictors, we categorized continuous variables to quartiles. The Kruskal-Wallis test provided means of comparing differences between these quartiles. The Mann-Whitney test permitted post hoc comparisons of each pair in groups after significant Kruskal-Wallis tests. We also used the Kruskal-Wallis test to see if there were differences between ASA scores and resource use (LOS), and for comparing differences in the sum of the ranks of continuous variables between patients with and without adverse outcomes. The Pearson chi-square test or Fisher's exact test (cell count ≤ 5) was used to used categorical variables related to dichotomized outcome. The Pearson chi-square

test with 2 × 2 contingency tables enabled the calculation of odds ratios with 95% confidence intervals, sensitivity, specificity, positive predictive value, and negative predictive value. Even though it was not our goal to identify single independent predictors, we also performed multivariable regression analyses. In all tests, p values < 0.05 were considered significant. The statistical analyses were carried out using IBM SPSS 21.0 statistical software for Mac OS X (version 21.0) and for Windows (version 21.0).

Results

A total of 644 patients underwent an elective craniotomy during the study period of nearly 13 months. The final study cohort consisted of 418 (75.9%) of 551 eligible

patients. The details on patient enrollment are presented in the study flow chart (Fig. 1).

Patient Characteristics

The mean and median ages of the 418 patients were 56.4 (SD 13.9 years) and 58.0 years (range 18 to 87 years), respectively, and 260 (62.2%) patients were female. In 124 cases (29.7%), patients were 65 years or older.

Craniotomies

The most common indications were a vascular lesion (for example, an aneurysm or arteriovenous malformation) in 138 (33.0%), a benign tumor in 134 (32.1%), and a malignant tumor in 121 (28.9%) of the 418 operations. The mean and median operation times (defined as the period from the time of the surgeon's first intervention, e.g., beginning of the sterile preparation until completion of the wound dressings) were 2 hours 40 minutes (SD 91.6 minutes) and 2 hours 8 minutes (range 42–767 minutes), respectively.

The mean and median general anesthesia times (defined as the time from the beginning of the administration of the first anesthetic agent until extubation or transfer to the ICU) were 3 hours 16 minutes (SD 93.2 minutes) and 2 hours 42 minutes (range 52–794 minutes), respectively. After the surgery, 57.3% of the extubations occurred in the operating room, and the remaining extubations took place in the ICU. For logistic reasons, transferring patients to the ICU before extubation is common at our clinic even in the case of uncomplicated surgical care or the absence of patient-related factors requiring prolonged intubation. Of all the patients, 94.7% were extubated within 6 hours after the end of surgery.

End Points

The in-hospital mortality rate was 1.0% (4 of 418 patients). In-hospital systemic or infectious complications occurred in 28 (6.7%) of 418 patients. In-hospital permanent or transient CNS deficits were recorded in 47 (11.2%)

FIG. 1. Flow chart of patient enrollment in the study.

TABLE 2. LOSs in the ICU and the hospital in all study patients, patients with systemic and infectious complications, and patients with CNS deficits

Patients	Mean ICU LOS in Days	Mean Hospital LOS in Days
All (n = 418)		
Mean ± SD	1.3 ± 1.4	5.6 ± 3.5
Median (range)	1.0 (0–13)	5.0 (1–34)
Systemic & infectious complications (n = 28)		
Mean ± SD	2.9 ± 3.5	9.8 ± 7.8
Median (range)	1.0 (0–13)	7.5 (2–34)
CNS deficits (n = 47)		
Mean ± SD	2.7 ± 3.5	7.0 ± 3.8
Median (range)	1.0 (1–13)	6.0 (2–17)

of 418 patients. Table 2 provides the ICU LOS and overall hospital LOS for all study patients and in the complication groups. Overall, 90.9% of the patients stayed 24 hours or less in the ICU. Most of the patients (84.7%) were discharged within the 1st postoperative week.

Single End Point Predictors in Univariate Analyses

Mortality

Given the limited number of in-hospital deaths (4 patients), no reliable predictors for mortality could be calculated. However, all 4 in-hospital deaths occurred in patients older than 65 years with a preoperative Helsinki ASA class of 3 or higher.

Morbidity

Older age (Tables 3–5), increased CRP (> 3 mg/L) (Tables 3 and 5), and the Helsinki ASA class (Table 5) were associated with in-hospital systemic and infectious complications. Patients with BMI values between 25.8 and 29.0 had more in-hospital systemic and infectious complications than patients in the lowest and highest quartiles (Table 4). No preoperative variable correlated with in-hospital permanent or transient CNS deficits (Tables 3–5).

Resource Use

Age ≥ 65 years and high Helsinki ASA class (> 2) were associated with increased resource use (Table 5). The oldest age group (66–87 years) stayed on average 1 day longer in the hospital than the youngest age group (18–47 years) (Table 6). Patients with preoperative blood glucose levels ≥ 6.7 mmol/L had a longer LOS in the ICU than patients with levels ≤ 5.7 mmol/L (Table 6). Patients with lowest (2.9–3.7 mmol/L) and highest (4.2–5.6 mmol/L) potassium levels also stayed longer in the ICU than patients with potassium levels 4.0 to 4.1 mmol/L (Table 6). Moreover, patients with the lowest hemoglobin levels (105–133 g/L) and patients with the highest systolic blood pressure values (156–224 mm Hg) seemed to be discharged marginally later than most of the other patients in the same group (Table 6).

Single End Point Predictors in Multivariable Analyses

Multivariable logistic regression analyses were conducted using variables that were found to be significant in the univariate analyses for morbidity (age, CRP, BMI, and Helsinki ASA class) and resource use (age, Helsinki ASA

TABLE 3. Preoperative patient-related factors, routine blood tests, and in-hospital outcome*

Factor	No. of Patients	Systemic & Infectious Complications			New CNS Deficits		
		Yes (range)	No (range)	p Value	Yes (range)	No (range)	p Value
Age (yrs)	418	64 (29–87)	56 (18–85)	0.002	58 (26–80)	56 (18–87)	0.138
Males	418	8.9%	91.1%	0.168	13.9%	86.1%	0.176
Females	418	5.4%	94.6%		9.6%	90.4%	
Weight (kg)	417	77 (52–107)	77 (40–164)	0.448	74 (44–164)	77 (40–155)	0.255
Height (cm)	416	172 (150–187)	169 (148–205)	0.176	170 (55–187)	169 (148–205)	0.832
BMI	416	26 (19–33)	27 (16–47)	0.943	26 (17–47)	27 (16–45)	0.140
SBP (mm Hg)	416	140 (104–197)	143 (95–224)	0.400	147 (108–201)	142 (95–224)	0.066
DBP (mm Hg)	416	85 (57–112)	86 (46–137)	1.00	87 (60–112)	86 (46–137)	0.270
HR (per min)	415	71 (47–111)	70 (41–114)	0.722	72 (49–97)	70 (41–114)	0.209
Hb (g/L)	417	137 (105–157)	141 (106–180)	0.509	140 (105–172)	141 (106–180)	0.937
Platelets (10 ⁹ /L)	417	241 (104–543)	246 (32–498)	0.308	247 (82–543)	245 (32–498)	0.994
Crea (μmol/L)	416	74 (43–107)	70 (5–160)	0.102	68 (43–108)	70 (5–160)	0.408
Gluc (mmol/L)	409	6.4 (4.6–10.5)	6.5 (3.9–24.8)	0.393	7.0 (4.5–24.5)	6.4 (3.9–24.8)	0.151
CRP (mg/L)	412	5.5 (3–16)	5.1 (3–77)	0.034	4.4 (3–25)	5.2 (3–77)	0.816
Na (mmol/L)	417	139 (126–146)	138 (123–158)	0.438	138 (127–146)	139 (123–158)	0.912
K (mmol/L)	417	4.1 (3.4–5.1)	4.0 (2.9–5.6)	0.068	4.0 (3.1–4.8)	4.0 (2.9–5.6)	0.423
PT (%)	410	109 (37–152)	112 (9–170)	0.591	111 (37–166)	112 (9–170)	0.965

Crea = plasma creatinine; DBP = diastolic blood pressure; Gluc = blood glucose (not fasting); Hb = plasma hemoglobin; HR = heart rate; K = plasma potassium; Na = plasma sodium; SBP = systolic blood pressure.

* Mean values are reported for continuous variables. The Mann-Whitney test was used for all variables except for sex, which was studied using the Pearson chi-square test. Values in boldface are statistically significant.

TABLE 4. Preoperative patient-related factors, routine blood tests, and in-hospital outcome*

Factor	No. of Patients	Systemic & Infectious Complications (%)	p Value	CNS Complications (%)	p Value
Age (yrs)	418		0.014†		0.343
18–47	105	2 (1.9)		10 (9.5)	
48–58	110	6 (5.5)		9 (8.2)	
59–65	93	6 (6.5)		11 (11.8)	
66–87	110	14 (12.7)		17 (15.5)	
Sex	418		0.168		0.176
Male	158	14 (8.9)		22 (13.9)	
Female	260	14 (5.4)		25 (9.6)	
Weight (kg)	417		0.454		0.596
40–64	97	5 (5.2)		12 (12.4)	
65–74	113	5 (4.4)		13 (11.5)	
75–86	104	9 (8.7)		14 (13.5)	
87–164	103	9 (8.7)		8 (7.8)	
Height (cm)	416		0.105		0.549
148–162	115	7 (6.1)		15 (13.0)	
163–169	96	2 (2.1)		7 (7.3)	
170–176	102	8 (7.8)		13 (12.7)	
177–205	103	11 (10.7)		12 (11.7)	
BMI	416		0.024‡		0.193
16.4–23.4	103	4 (3.9)		14 (13.6)	
23.5–25.7	105	8 (7.6)		12 (11.4)	
25.8–29.0	104	13 (12.5)		15 (14.4)	
29.1–47.4	104	3 (2.9)		6 (5.8)	
SBP (mm Hg)	416		0.842		0.063
95–128	106	9 (8.5)		9 (8.5)	
129–141	103	6 (5.8)		9 (8.7)	
142–155	105	6 (5.7)		10 (9.5)	
156–224	102	7 (6.9)		19 (18.6)	
DBP (mm Hg)	416		0.615		0.700
46–78	101	8 (7.9)		10 (9.9)	
79–86	113	5 (4.4)		11 (9.7)	
87–93	105	9 (8.6)		12 (11.4)	
94–137	97	6 (6.2)		14 (14.4)	
HR (per min)	415		0.542		0.387
41–60	106	6 (5.7)		9 (8.5)	
61–68	102	7 (6.9)		11 (10.8)	
69–78	104	10 (9.6)		10 (9.6)	
79–114	103	5 (4.9)		16 (15.5)	
Hb (g/L)	417		0.841		0.708
105–133	108	8 (7.4)		14 (13.0)	
134–140	100	7 (7.0)		8 (8.0)	
141–147	104	5 (4.8)		12 (11.5)	
148–180	105	8 (7.6)		12 (11.4)	
Platelets (10 ⁹ /L)	417		0.349		0.400
32–201	104	6 (5.8)		14 (13.5)	
202–238	105	11 (10.5)		7 (6.7)	
239–285	103	6 (5.8)		13 (12.6)	
286–543	105	5 (4.8)		12 (11.4)	

(continued)

TABLE 4. Preoperative patient-related factors, routine blood tests, and in-hospital outcome* (continued)

Factor	No. of Patients	Systemic & Infectious Complications (%)	p Value	CNS Complications (%)	p Value
Crea ($\mu\text{mol/L}$)	416		0.290		0.428
5–59	104	5 (4.8)		15 (14.4)	
60–68	106	5 (4.7)		10 (9.4)	
69–77	102	7 (6.9)		8 (7.8)	
78–160	104	11 (10.6)		13 (12.5)	
Gluc (mmol/L)	409		0.701		0.337
3.9–5.3	111	5 (4.5)		10 (9.1)	
5.4–5.7	87	6 (6.9)		9 (10.3)	
5.8–6.6	105	7 (6.1)		10 (9.5)	
6.7–24.8	106	9 (9.3)		17 (16.0)	
Na (mmol/L)	417		0.077		0.842
123–136	92	8 (8.7)		10 (10.9)	
137–139	143	4 (2.8)		14 (9.8)	
140	56	3 (5.4)		8 (14.3)	
141–148	126	13 (10.3)		14 (11.1)	
K (mmol/L)	417		0.178		0.297
2.9–3.7	91	5 (5.5)		14 (15.4)	
3.8–3.9	106	5 (4.7)		11 (10.4)	
4.0–4.1	102	5 (4.9)		7 (6.9)	
4.2–5.6	118	13 (11.0)		14 (11.9)	
PT (%)	410		0.645		0.715
9–96	104	8 (7.7)		9 (8.7)	
97–108	103	8 (7.8)		14 (13.6)	
109–128	100	4 (4.0)		12 (12.0)	
129–170	103	8 (7.8)		11 (10.7)	

* Continuous variables were divided into fourths on the basis of quartiles. CRP could not be divided since three-quarters of the patients had CRP less than 4 mg/L. The Pearson chi-square test was used to test for independence. The post hoc test for the significant results was done on each pair using the Pearson chi-square 2×2 contingency table. Values in boldface are statistically significant.

† Youngest age group (18–47 years) differed from the oldest (66–87 years) age group ($p = 0.003$).

‡ Lowest (16.4–23.4) and highest (29.1–47.4) BMI groups differed from the 3rd BMI group (25.8–29.0) ($p = 0.024$ and $p = 0.009$, respectively).

class, systolic blood pressure, hemoglobin, glucose, and potassium). For systemic and infectious complications, CRP remained significant after bivariate logistic regression analyses only when treated as a categorized (dichotomized) covariate, whereas age retained its significance whether treated as a categorical or a continuous covariate (results not shown). Helsinki ASA classification (categorical) also remained significant in all possible multivariable regression analyses (results not shown). Using linear regression analyses for continuous outcome variables, Helsinki ASA classification (categorical) was the only variable that remained a significant predictor for both ICU LOS and hospital LOS (results not shown).

Composite End Point Predictor

Various combinations of significant end point predictors were evaluated for the identification of high-risk patients for complications and increased resource use (results not shown). Almost one-fourth of the patients with Helsinki ASA Class 4, age ≥ 60 years, and CRP values > 3 mg/L had systemic or infectious complications after cranial surgery, with up to nearly 5 times higher odds ratios (Table

7). If a patient ≥ 60 years had a preoperative Helsinki ASA class of 4, the LOS in the ICU was nearly 40% and in hospital approximately 20% longer than in patients without this combination of factors (Table 8).

Discussion

In this first prospective study on outcome predictors in an unselected cohort of patients undergoing cranial neurosurgery, higher Helsinki ASA class (> 2), increased age (> 60 –65 years) and abnormal CRP values (> 3 mg/L) predicted postoperative in-hospital systemic and infectious complications. A composite factor of the Helsinki ASA class, age, and CRP value identified patients with up to nearly 5 times higher odds ratios for postoperative systemic and infectious complications preoperatively (Table 7). In other words, it was able to identify almost every fourth patient with major postoperative systemic or infectious complications (Table 7). The composite factor also predicted a prolonged stay in the ICU (Table 8). No preoperative assessment parameter predicted postoperative CNS complications, which probably are more lesion and surgeon-related complications than systemic and infectious

TABLE 5. Major risk predictors and study end points*

Factor	No. of Patients (%)	Systemic & Infectious Complications		p Value	New CNS Deficits		p Value	ICU LOS (days)	p Value	Hospital LOS (days)		p Value
		Yes (%)	No (%)		Yes (%)	No (%)						
ASA class				0.213			0.408		0.095			0.389
1	67 (16.1)	2 (3.0)	65 (97.0)		7 (10.4)	60 (89.6)		1.09		5.12		
2	152 (36.5)	8 (5.3)	144 (94.7)		19 (12.5)	133 (87.5)		1.42		5.53		
3	166 (39.8)	14 (8.4)	152 (91.6)		15 (9.0)	151 (91.0)		1.16		5.64		
4	32 (7.7)	4 (12.5)	28 (87.5)		6 (18.8)	26 (81.3)		1.84		6.34		
Helsinki ASA class				0.021†			0.663		0.036‡			0.007§
1	4 (1.0)	0	4 (100.0)		0	4 (100.0)		1.0		4.0		
2	94 (22.5)	1 (1.1)	93 (98.9)		9 (9.6)	85 (90.4)		1.12		4.82		
3	251 (60.2)	18 (7.2)	233 (92.8)		28 (11.2)	223 (88.8)		1.22		5.65		
4	68 (16.3)	9 (13.2)	59 (86.8)		10 (14.7)	58 (85.3)		1.87		6.35		
Age in yrs				0.004			0.169		0.027			0.008
≥65	124 (29.7)	15 (12.1)	109 (87.9)		18 (14.5)	106 (85.5)		1.35		6.06		
<65	294 (70.3)	13 (4.4)	281 (95.6)		29 (9.9)	265 (90.1)		1.28		5.36		
CRP in mg/L				0.046			0.835		0.689			0.889
>3	106 (25.7)	11 (10.4)	95 (89.6)		11 (10.4)	95 (89.6)		1.32		5.60		
≤3	306 (74.3)	15 (4.9)	291 (95.1)		34 (11.1)	272 (88.9)		1.25		5.34		

* The Pearson chi-square test was used for 2×2 and $2 \times k$ contingency tables of categorical variables. The Kruskal-Wallis test was used for studying differences in LOS. The post hoc Mann-Whitney test was used on each pair of significant groups. Values in boldface are statistically significant.

† ASA Helsinki Class 2 differed from ASA Helsinki Classes 3 ($p = 0.027$) and 4 ($p = 0.002$).

‡ ASA Helsinki Class 4 differed from ASA Helsinki Classes 2 ($p = 0.015$) and 3 ($p = 0.013$).

§ ASA Helsinki Class 2 differed from ASA Helsinki Classes 3 ($p = 0.022$) and 4 ($p = 0.001$).

complications. Focusing on the preoperative identification of patients susceptible to in-hospital complications was the rationale behind the decision not to focus and report on numerous other perioperative factors that may contribute to outcome, such as the choice of anesthetic agent, intraoperative temperature control, type of antibiotic prophylaxis, or postoperative analgesia. In brief, it is practically impossible to control all theoretical confounding factors in similar outcome studies. Furthermore, these results are in keeping with the findings based on the recent systematic review, suggesting that preoperative ASA class can be useful in predicting other than lesion and surgeon-related complications.⁹

Role of Study Design and Clinical Applicability

An era of big data analyses in health care has already started. Despite the potential benefits of the big data revolution, the value of any results relies on validity of the data used. When identifying new associations with surgical outcomes, most large registries and databases cannot provide us with detailed and useful results. In the recent retrospective study of more than 10,000 cranial neurosurgery patients,¹⁰ the incomplete reflection of patient characteristics obtained from the database as well as the lack of fit for the complications unique to neurosurgical patients hindered the identification of useful predictors for adverse outcome, as discussed by the authors. Furthermore, the reliability of evaluating the quality of care based on such registries is compromised by the rarity of outcome events along with the low caseload in many individual hospitals.⁵ Considering the low rates of morbidity and mortality in

modern cranial neurosurgery, identifying single independent outcome predictors was beyond the scope of our study. Instead, we aimed to find a preoperative composite factor that should act as a red flag and suggest a more thorough evaluation and individually tailored perioperative plan for patients at high risk for postoperative systemic and infectious complications in an unselected cohort of patients undergoing elective cranial neurosurgery. Identifying a preoperative composite factor with a reasonable positive predictive value can be sensible even in low caseload units, since it seems unlikely that a single preoperative outcome predictor for all neurosurgical patients would be found.

ASA Class and Composite Preoperative End Point Predictor

The ASA Physical Status Classification system was first introduced in the 1940s and revised in 1963, and it is the most widely known and used system for preoperative risk assessment.^{1,11} The Helsinki ASA modification implemented approximately 2 decades ago was based on clinical observations and judgments by neuroanesthesiologists. Ever since, it has been used without a proper validation. Our study suggests that this call was justified, even though the precise criteria for the change are largely unknown. However, the modification takes into account some of the characteristics of the unique patient population in cranial neurosurgery, and these characteristics are embedded in the Helsinki ASA class but not in the original ASA class. Bearing in mind the original purpose of the ASA classification, the ASA class should perhaps be seen more as a representative of the burden of systemic disease at a given

TABLE 6. Preoperative patient-related factors, routine blood tests, and LOS*

Factor	No. of Patients	LOS in ICU	p Value	LOS in hospital	p Value
Age (yrs)	418		0.303		0.029†
18–47	105	1.2		4.9	
48–58	110	1.4		5.3	
59–65	93	1.4		6.3	
66–87	110	1.3		4.9	
Sex	418		0.861		0.496
Male	158	1.4		5.6	
Female	126	1.3		5.6	
Weight (kg)	417		0.145		0.191
40–64	97	1.4		6.0	
65–74	113	1.2		5.4	
75–86	104	1.2		5.6	
87–164	103	1.4		5.4	
Height (cm)	416		0.667		0.112
148–162	115	1.4		6.0	
163–169	96	1.2		4.8	
170–176	102	1.2		5.6	
177–205	103	1.5		5.7	
BMI	416		0.406		0.545
16.4–23.4	103	1.4		5.9	
23.5–25.7	105	1.4		5.8	
25.8–29.0	104	1.2		5.3	
29.1–47.4	104	1.2		5.2	
SBP (mm Hg)	416		0.189		0.029‡
95–128	106	1.1		5.3	
129–141	103	1.3		5.1	
142–155	105	1.2		5.7	
156–224	102	1.5		6.2	
DBP (mm Hg)	416		0.556		0.914
46–78	101	1.2		5.4	
79–86	113	1.1		5.6	
87–93	105	1.4		5.7	
94–137	97	1.4		5.6	
HR (per min)	415		0.343		0.387
41–60	106	1.1		5.7	
61–68	102	1.2		5.6	
69–78	104	1.3		5.7	
79–114	103	1.5		5.2	
Hb (g/L)	417		0.317		0.019§
105–133	108	1.4		6.2	
134–140	100	1.2		5.0	
141–147	104	1.3		5.6	
148–180	105	1.3		5.5	

(continued)

moment, not as a predictor of perioperative in-hospital neurological deficits. Our study results align with this view, as the preoperative Helsinki ASA score correlated with postoperatively recorded systemic and infectious

TABLE 6. Preoperative patient-related factors, routine blood tests, and LOS* (continued)

Factor	No. of Patients	LOS in ICU	p Value	LOS in hospital	p Value
Platelets (10 ⁹ /L)	417		0.416		0.500
32–201	104	1.3		5.8	
202–238	105	1.2		5.5	
239–285	103	1.2		5.4	
286–543	105	1.3		5.6	
Crea (μmol/L)	416		0.143		0.729
5–59	104	1.4		5.6	
60–68	106	1.1		5.7	
69–77	102	1.4		5.7	
78–160	104	1.3		5.4	
Gluc (mmol/L)	409		0.012¶		0.485
3.9–5.3	111	1.1		5.7	
5.4–5.7	87	1.2		5.5	
5.8–6.6	105	1.4		5.6	
6.7–24.8	106	1.5		5.5	
Na (mmol/L)	417		0.117		0.295
123–136	92	1.5		6.5	
137–139	143	1.2		5.2	
140	56	1.4		5.0	
141–148	126	1.3		5.6	
K (mmol/L)	417		0.025**		0.826
2.9–3.7	91	1.3		5.2	
3.8–3.9	106	1.3		6.0	
4.0–4.1	102	1.2		5.1	
4.2–5.6	118	1.4		5.9	
PT %	410		0.746		0.293
9–96	104	1.1		4.9	
97–108	103	1.5		6.3	
109–128	100	1.2		5.5	
129–170	103	1.3		5.7	

* Continuous variables were divided into fourths (quartiles). CRP values could not be divided into fourths since three-fourths of the patients had normal CRP values (≤ 3 mg/l). The Kruskal-Wallis test was used to study differences between fourths. The post hoc Mann-Whitney test was used on each pair of significant groups. Values in boldface are statistically significant.

† Age group 4 (66–87 years) differed from age groups 1 (18–47 years; $p = 0.019$) and 2 (48–58 years; $p = 0.020$).

‡ SBP group 2 (129–141 mm Hg) differed from SBP group 4 (156–224 mm Hg; $p = 0.004$).

§ Hb group 1 (105–133 g/L) differed from Hb groups 2 (134–140 g/L; $p = 0.010$) and 4 (148–180 g/L; $p = 0.013$).

¶ Blood glucose level group 4 (6.7–67.0 mmol/L) differed from blood glucose level groups 1 (3.9–5.3 mmol/L; $p = 0.009$) and 2 (5.4–5.7 mmol/L; $p = 0.020$).

** Potassium level group 3 (4.0–4.1 mmol/L) differed from groups 1 (2.9–3.7 mmol/L; $p = 0.033$) and 4 (4.2–5.6 mmol/L; $p = 0.003$).

complications but not with new or worsening neurological deficits. Quantification of the systemic and infectious postoperative risks and making that quantification a part of surgical decision making may guide the selection of the safest treatment modality and resource allocation for an individual patient. For resource management, the use of

TABLE 7. Various combinations of risk predictors and systemic and infectious complications

Combinations	No. of Patients	OR (95% CI)	p Value*	PPV	NPV	Spec	Sens
Combination 1: Helsinki ASA Class 4 & age ≥ 60 yrs	44	3.93 (1.62–9.57)	0.001	18.2%	94.7%	90.8%	28.6%
Combination 2: Helsinki ASA Class 4, & age ≥ 60 yrs, & CRP > 3 mg/L	17	4.82 (1.46–15.91)	0.005	23.5%	94.0%	96.7%	14.3%
Combination 3: Helsinki ASA Class 4 & CRP > 3 mg/L	28	2.54 (0.81–7.90)	0.097	14.3%	93.8%	93.8%	14.3%

NPV = negative predictive value; PPV = positive predictive value; sens = sensitivity; spec = specificity.

* Boldface indicates statistical significance.

a simple combination of preoperative factors can provide a tool to estimate the overall hospital costs for each patient. For example, the combination of Helsinki ASA Class 4 and age ≥ 60 years carries an estimated extra cost of €1500–€2800 per patient during the in-hospital period at our institution. The combination of Helsinki ASA class, age, and CRP in risk prediction needs to be validated in a different cohort of elective craniotomy patients in the future. Combining Helsinki ASA Classes 1 and 2 may be appropriate, since only 4 patients (1%) were classified as Helsinki ASA Class 1 in this study.

Strengths and Weaknesses of the Study

The study may have a few advantages. The study was based on assessments made by anesthesiologists, who apparently have no incentives to manipulate any of the study measures. In addition to the prospective study design, the broad inclusion criteria probably increase the external validity of the results: i.e., these results may be applicable to many Western neurosurgical units. There are also some limitations and drawbacks to this study. Regardless of its simplicity and wide applicability, the original ASA Physical Status Classification has been criticized for its considerable interrater variability.^{2,6,8} The Helsinki ASA classification may suffer from the same limitation. Most importantly, the Helsinki ASA system has not been validated previously, and therefore it may represent an institution-specific phenomenon.

Unfortunately, the scope of the study failed to include determining the interrater variability of the original or Helsinki ASA classifications, so we cannot exclude the possibility that the Helsinki ASA classification is subject to variability, or that it is institutionally biased. However, detailed instructions on determining both ASA classifications were implemented in the study protocol, and the Helsinki ASA classification is comparable to the original ASA classification in terms of its applicability in a clinical scenario. The study can also be criticized for being underpowered and susceptible to statistical errors. Our data were prospectively collected and tailored to the specific characteristics of intracranial neurosurgery and represent a full year's case mix at our institution. Moreover, the objective was not to evaluate the predictive value of single independent factors but rather to find a combination, i.e., a new widely applicable composite factor, which is associated with a greater risk of in-hospital complications. We aimed at simplicity in our statistical approach, but multivariable regression analyses were performed to supplement the analyses. As another possible drawback, patients' comorbidities were not included as possible contributors to outcome, similar to the previous registry-based study.¹⁰ The main reason for excluding such data in the analyses was to increase the external validity of the results. In addition to highly varying incidences and prevalence, comorbidities, such as hypertension, myocardial disease, and renal insufficiency, are diagnosed and treated differently in different countries and institutions, and thus inclusion of these data would probably decrease the generalizability of the results. Furthermore, ASA classification indirectly includes the patient's comorbidity status. As our main purpose was to study the general applicability of various anesthesiological preoperative assessments in predicting in-hospital outcome, the use of perioperative surgical parameters (such as surgeon's experience, location of the lesion, preoperative diagnosis, surgical positions, and surgical time) as study inclusion criteria was deemed unnecessary. Furthermore, these factors are absent in previously published outcome scores.⁹ In addition, the presented predictors of outcome (i.e., the Helsinki ASA class, age, and CRP) are relatively objective and applicable in most Western countries with life expectancies similar to those in Finland. Finally, the low mortality and morbidity rates can perhaps be considered major drawbacks of our study, as statistical analyses on mortality-associated factors were unreliable, and no detailed subgroup analyses could be performed on the morbidity-related predictors. This may also have

TABLE 8. Various combinations of risk predictors and resource use

Combination*	No. of Patients	Mean ICU LOS	p Value†	Mean Hospital LOS	p Value†
Combination 1			0.018		0.004
Yes	44	1.95		6.86	
No	374	1.22		5.41	
Combination 2			0.164		0.216
Yes	17	2.12		6.71	
No	400	1.26		5.52	
Combination 3			0.077		0.135
Yes	28	1.82		6.25	
No	389	1.26		5.52	

* Combination 1: Helsinki ASA Class 4 and age ≥ 60 years; Combination 2: Helsinki ASA = 4, age ≥ 60 years, and CRP > 3 mg/L; and Combination 3: Helsinki ASA Class 4 and CRP > 3 mg/L.

† Boldface indicates statistical significance.

contributed to the fact that none of the factors assessed in this study predicted new neurological deficits.

Conclusions

Our results suggest that using a simple composite factor as a risk estimate of complications and resource use, health care professionals may be able to preoperatively identify patients requiring extra cautions and tailored care. Contrary to the traditional view that the location and nature of the lesion and the expertise of the surgeon determine the risk of an adverse outcome in brain surgery, our results suggest that it is possible to identify patients prone to systemic and infectious complications with simple preoperative assessments. Even though large registry-based studies are plausible also in Finland, a customized prospective study setting is imperative in establishing the value of preoperative factors in predicting postoperative complications. When such prospective studies are piloted in large neurosurgical centers, nationwide and international multicenter studies can be implemented to substantiate the findings. Thus, the results and morbidity rates presented here may perhaps serve as first objective benchmark numbers in the modern neurosurgical era and a guide to safeguarding good practice.

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Supplemental Information

Previous Presentation

The results of this study were presented in part in abstract/poster form at Euroanaesthesia 2013 in Barcelona, Spain, June 4, 2013, and at the 32nd Scandinavian Society of Anaesthesiology and Intensive Care Medicine Congress in Turku, Finland, August 28, 2013.

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