Notwendigkeit und Umfang der postoperativen intensiv-medizinischen Überwachung von Patienten nach elektiven epilepsiechirurgischen Eingriffen

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Abkürzungsverzeichnis

ASA	American Society of Anesthesiologists
BMI	Body-Mass-Index
DM	Diabetes Mellitus

1. Deutsche Zusammenfassung

1.1 Einleitung

Temporallappenepilepsie ist eine der häufigsten Formen der fokalen Epilepsien bei Erwachsenen (Wiebe, 2000). Trotz teilweise langjähriger Behandlung mit antikonvulsiven Medikamenten in der Regel sogar als Kombination aus mindestens zwei oder mehreren geeigneten Präparaten, entwickeln ungefähr 30 % bis 40 % dieser Patienten eine sogenannte medikamenten-resistente Epilepsie (Wiebe, 2013). In dieser Patientengruppe erfolgt normalerweise weitere nicht-invasive und ggf. invasive Untersuchungen zur Evaluation eines möglichen kurativen oder palliativen epilepsiechirurgischen Eingriffs (Rugg-Gunn et al., 2020). Nach erfolgtem elektiven resektiven epilepsiechirurgischen Eingriff werden die Patienten üblicherweise postoperativ auf einer (Neuro)-Intensivstation überwacht. Hiervon verspricht man sich eine engmaschige klinische und neurologische Überwachung der Patienten im unmittelbaren postoperativen Verlauf mit dem Ziel einer frühzeitigen Erkennung von postoperativen lebensbedrohlichen Komplikationen oder klinischen Ereignissen, welche eine schnelle medizinische oder chirurgische Intervention benötigen. Die aktuelle Datenlage zeigt hingegen, dass Patienten, die sich einem elektiven supratentoriellen Eingriff unterziehen, selten Komplikationen entwickeln, welche eine intensivmedizinische Überwachung notwendig machen (Badenes et al., 2017; Bui et al., 2011). Außerdem zeigen aktuelle Studien, dass die krankenhaus-abhängige Komplikationen durch zügige angemessene Verlegung der Patienten auf eine Normalstation sowie frühe Mobilisation der Patienten signifikant reduziert werden können (Laan et al., 2020; Wagner et al., 2003).

Grundlegend wird der Erfolg eines epilepsiechirurgischen Eingriffs sowohl anhand der postoperativen Anfallsfreiheit als auch anhand der postoperativen klinischen und neurologischen Ergebnisse bemessen. Daher stellt die angemessene postoperative Überwachung diesen Patienten einen wichtigen Aspekt in der Sicherung eines guten postoperativen klinischen und neurologischen Erfolges dar. Auf der anderen Seite stellen epilepsiechirurgische Patienten aufgrund des relativ jungen Patientenalters und

der wenigen Komorbiditäten eine spezifische und relativ homogene Subgruppe der Patienten dar, die sich einem elektiven supratentoriellen neurochirurgischen Eingriff unterziehen (d' Orio et al., 2017; Engel, 2019).
Ferner zeigt die aktuelle Covid-19-Pandemie, dass eine vorausschauende Verwaltung der medizinischen Ressourcen - und v.a. der Ressourcen der Intensivstationen, von enormer Bedeutung ist (Bartsch et al., 2020; Leclerc et al., 2020).
Vor diesem Hintergrund und, um auf die klinische Fragestellung zur Notwendigkeit einer intensivmedizinischen Überwachung nach einem elektiven epilepsiechirurgischen Eingriff eine Antwort zu liefern, haben wir eine retrospektive Studie mit den institutseigenen Daten durchgeführt. In dieser Analyse haben wir die Häufigkeit des Auftretens von Ereignissen, welche eine intensiv-medizinische Überwachung erforderten, sowie die dazu beitragenden möglichen prä- und intraoperativen Faktoren untersucht.

1.2 Methoden

Über das Krankenhausinformationssystem wurden die Daten aller Patienten mit pharmako-resistenten Epilepsie, die sich im Zeitraum vom 2012 bis 2019 in der Neurochirurgischen Klinik des Universitätsklinikums Bonn einem elektiven, resektiven epilepsiechirurgischen Eingriff unterzogen (n=266), erhoben und analysiert.

Hierbei wurden Informationen bzgl. der Patientencharakteristika zum Zeitpunkt der Aufnahme, der Art des chirurgischen Eingriffs sowie des intraoperativen Verlaufs (Operationsdauer, Blutverlust, Transfusion von Blut und Blutprodukten sowie intraoperativen chirurgischen Besonderheiten) erfasst und analysiert.

Die Ausschlusskriterien sind: 1) Alter < 18; 2) Patienten, bei denen eine funktionelle Hemisphärektomie durchgeführt wurde; 3) Invasiven diagnostischen Eingriffe.

Bei allen in die Analyse eingeschlossenen Patienten erfolgte prächirurgisch eine umfangreiche standardisierte epileptologische Diagnostik. Diese umfasst eine eingehende neurologische Untersuchung, Erhebung der Anfallssemiologie, ein Langzeit-Video-EEG, eine MRT-Untersuchung und ggf. weitere bildgebende Diagnostik. In den

Fällen mit inkongruenten elektro-klinischen oder bildgebenden Befunden erfolgte eine invasive prächirurgische Evaluation durch Implantation von Tiefenelektroden. Anschließend wurde in jedem einzelnen Fall die Indikation zur Durchführung eines resektiven epilepsiechirurgischen Eingriffs i.R. der interdisziplinären Epilepsiechirurgischen Konferenz individuell gestellt.

Postoperativ erfolgte die initiale Überwachung im Aufwachraum und im Anschluss auf der Neuro-Intensivstation. Die definierten Überwachungsparameter sind: Sauerstoffsättigung, Herzfrequenz, nicht-invasive Blutdruckmessung sowie regelmäßige neurologische Untersuchung (Pupillenmotorik, Bewusstseinslage und grobe Motorik der Extremitäten) durch geschulte Fachpflegekräfte.

Folgende Ereignissen innerhalb von 48 Stunden postoperativ, welche eine intensivmedizinischen Überwachung erfordern bzw. rechtfertigen, wurden definiert: 1) Abfall des Glasgow Coma Scores von >2; 2) früher postop. generalisierter Krampfanfall; 3) die Notwendigkeit einer Revision-OP bei neurologisch-relevanter Nachblutung; 4) die Notwendigkeit einer Re-Intubation; 5) klinisch relevanter ischämischer Schlaganfall; 6) akutes Koronarsyndrom; 7) Kardiopulmonale Reanimation; 8) die Notwendigkeit einer Katecholamin-Therapie aufgrund eines kurzfristigen postoperativen Volumenmangels oder hämodynamischer Instabilität; 9) die Notwendigkeit einer intravenösen Insulin-Therapie aufgrund einer postoperativen hyperglykämischen Entgleisung.

Zur statistischen Auswertung wurde die SPSS Software (Version 25, IBM Corp., Armonk, NY) verwendet. Die Häufigkeitsverteilung sind als Mittelwert mit Standardabweichung angegeben. Die kategorialen Variablen wurden mittels Fisher-Test, die kontinuierlichen Variablen mittels Mann-Whitney U-Test verglichen. Die Area Under the Curve (AUC), Spezifität und Sensitivität sowie die Cut-off-Werte der statistisch signifikanten kontinuierlichen Variablen wurden mittels Receiver Operating Characteristic Curve (ROC) bestimmt. Eine multivariate binär logistische Regressionsanalyse wurde zur Identifikation von unabhängigen signifikanten Einflussfaktoren durchgeführt. Hierzu wurden nur die Variablen, die einen signifikanten Einfluss in der univariaten Analyse aufwiesen, untersucht. In allen statistischen Analysen wurde ein Signifikanzwert ($p < 0.05$) als statistisch signifikant gewertet.

1.3 Ergebnisse

In einem zuvor definierten Zeitraum wurden 266 Patienten mit pharmako-resistenten Epilepsie, die sich einem elektiven resektiven epilepsiechirurgischen Eingriff unterzogen, identifiziert. Davon entwickelten 13 Patienten innerhalb von 48h postoperativ mindestens ein Ereignis, welches eine intensiv-medizinische Überwachung erforderte (Gruppe I). Die restlichen 253 Patienten hatten einen unauffälligen postoperativen Verlauf (Gruppe II). Die detaillierten Ergebnisse über die patienten-charakteristische Daten sowie intraoperativen Verlauf sind in der Tabelle 1 der Originalpublikation aufgelistet.

Bei 116 von 266 Patienten erfolgte eine transsylvische selektive Amygdala-Hippokampektomie. Eine Temporalpol-Resektion erfolgte in 34 Fällen. Bei 22 Patienten wurde eine temporale Läsionektomie mit Amygdala-Hippokampektomie und bei 36 Patienten eine temporale Läsionektomie ohne Amygdala-Hippokampektomie durchgeführt. Bei 58 von 266 Patienten wurde eine extra-temporale Läsionektomie durchgeführt (s. FIG. 1 in Bahna et al., 2022).

Bezogen auf dem postop. Verlauf, zeigte sich die Notwendigkeit eines Revisionseingriffes aufgrund einer relevanten Nachblutung bei 5 Patienten als das am häufigsten aufgetretenes Ereignis, welches eine intensiv-medizinische Überwachung erforderte. Die detaillierte Häufigkeit der aufgetretenen Ereignisse sind in der Tabelle 2 der Originalpublikation aufgelistet. Die Krankenhausmortalität lag bei 0 %. Außerdem wurde das Auftreten vom akuten Koronarsyndrom, die Notwendigkeit einer Kardiopulmonalen Reanimation oder Re-Intubation nicht beobachtet.

Die Mehrheit der Patienten der Gruppe I entwickelten ein Ereignis, welches eine intensiv-medizinische Überwachung erforderte, innerhalb der ersten 24 Stunden postoperativ (12 von 13 Patienten).

Es zeigten sich keine statistisch signifikanten Unterschiede in der Verteilung der demografischen Daten (Alter und Geschlecht sowie Durchschnittsalter bei der Operation und Epilepsie-Dauer) zwischen beiden Gruppen. Bezogen auf die Komorbiditäten,

zeigte sich eine starke Assoziation zwischen dem Auftreten von frühen postoperativen Komplikationen und Diabetes Mellitus (DM) (33.3 % vs. 4.2 %; p=0.03) Sowie Body-Mass-Index (BMI) > 30 (12.8 % vs. 3.2 %; p=0.014).

Bezogen auf den intraop. Verlauf, zeigte sich eine starke Assoziation zwischen den Fällen, bei denen intraoperativ durch den Chirurgen von diffusen Blutungsneigung ohne sichtbare Gefäßverletzung oder laborchemisch fassbaren Gerinnungsstörungen im OP-Bericht berichtet wurde, und dem Auftreten von frühen postoperativen Ereignissen, welche eine intensiv-medizinische Überwachung erforderten, (p=0.013). Die durchgeführte ROC-Analyse konnte einen signifikanten Zusammenhang zwischen dem intraoperativen Blutverlust von mehr als 325 mL und dem Auftreten von frühen postoperativen Ereignissen mit Inanspruchnahme von intensiv-medizinischen Ressourcen zeigen (AUC: 0.766, p = 0.001, Sensitivität 76.9 %, Spezifität 77.7 %).

Schließlich zeigte die multivariate binär logistische Regressionsanalyse, dass DM (p = 0.029, OR 9.2, 95 % CI 1.26 - 67.5) sowie ein intraop. Blutverlust ≥ 325 mL (p = 0.012, OR 6.2, 95 % CI 1.5 – 26) unabhängige Prädiktoren für die Notwendigkeit einer postoperativen intensiv-medizinischen Überwachung sind (s. TABLE 3 in Bahna et al., 2022).

1.4 Diskussion

Das klinische Outcome nach einem resektiven epilepsiechirurgischen Eingriff wird anhand der Anfallsfreiheit sowie den postoperativen klinischen und neurologischen Befunden bewertet. Bezogen auf das postoperative Outcome, zeigen verschiedene Studien auf der einen Seite, dass durch eine Überwachung auf der Neuro-Intensivstation die Krankenhausmortalität bei Patienten mit Schädel-Hirn-Trauma oder intrakraniellen Blutung gesenkt werden könnte (Diringer und Edwards, 2001; Mirski et al., 2001; Varelas et al., 2008). Auf der anderen Seite gelten resektive epilepsiechirurgische Eingriffe als sehr standardisiert und sicher (Engel, 2018; Engel et al., 2012; Wiebe et al., 2001). Zudem zeigen aktuelle Daten, dass Krankenhausmortalität bei Patienten, die sich z.B. einer Temporallappenresektion

unterzogen haben, bei 1,4 % und die Rate an postoperativen sogenannten Major-Komplikationen bei 6,5 % liegt. Ferner zeigt die Arbeit von d'Orio et al., dass die allgemeinen chirurgie-abhängige Komplikationen bei Patienten im Alter von über 50 Jahren, die sich einem epilepsiechirurgischen Eingriff unterzogen haben, bei 10 % liegt (d' Orio et al., 2017; Kerezoudis et al., 2018; Schmidt et al., 2016). In unserem Patientenkollektiv konnte eine 0 % Krankenhausmortalität von 0 % sowie eine Rate von 4.9 % an frühen postoperativen Ereignissen, welche eine intensiv-medizinische Überwachung erforderten, beobachtet werden.

Insgesamt erfolgte bei 1.9 % der Patienten in unserem Kollektiv eine Revisions-OP aufgrund einer klinisch relevanten postoperativen Nachblutung. Basali et al. fanden eine Korrelation zwischen den frühen postoperativen erhöhten Blutdruckwerten (syst. Blutdruck > 160 mmHg oder diast. Blutdruck > 90 mmHg) und dem Auftreten von postoperativen relevanten Nachblutungen. Dabei hatten 62 % der untersuchten Patienten mit intrakraniellen Nachblutung erhöhten Blutdruckwerten im Vergleich zu den 25 % der untersuchten Patienten, die keine relevante Nachblutung entwickelten (Basali et al., 2000). Diesbezüglich zeigten unsere Daten, dass 21 von 266 Patienten (7.9 %) kurzfristig postoperativ eine intravenöse antihypertensive Medikation brauchten. Da die intravenöse antihypertensive Medikation in unserer Klinik ebenfalls auf der neurochirurgischen IMC-Station applizierbar ist, wurde dies in unserer Arbeit nicht als ein intensivmedizin-relevantes Ereignis definiert. Im Gegensatz dazu ist die intravenöse Applikation von Katecholaminen in unserer Klinik nur auf der Intensivstation durchführbar. Vier von 266 Patienten (1.5 %) brauchten eine intravenöse Katecholamin-Therapie aufgrund einer kurzfristigen postoperativen hämodynamischen Instabilität am ehesten bei Volumenmangel.

Eine Normoglykämie ist aufgrund ihrer neuroprotektiven Wirkung (Huttner, 2018) ein wichtiger Aspekt in der neurologischen Intensivmedizin. Aktuelle Studien zeigen, dass eine hyperglykämischen Entgleisung einen negativen Effekt auf das Outcome von Patienten mit einem Schädel-Hirn-Trauma oder einem ischämischen Stroke hat (Bilotta et al., 2008; Luitse et al., 2017; Svedung Wettervik et al., 2019). Darüber hinaus ist eine Assoziation mit erhöhtem Risiko von Vasospasmen bei Patienten mit Subarachnoidalblutung in der Literatur beschrieben (Inagawa et al., 2014). Bezüglich

des Auftretens von postoperativen Komplikationen nach einem elektiven supratentoriellen neurochirurgischen Eingriff scheint Diabetes mellitus ein klar identifizierbarer Risikofaktor in vielen Studien zu sein (Beauregard und Friedman, 2003; Hanak et al., 2014; Rolston et al., 2014). Im Einklang mit diesen Ergebnissen, zeigt unsere multivariate Analyse eine signifikante Assoziation zwischen DM und der Notwendigkeit einer postoperativen intensivmedizinischen Überwachung.

Ferner zeigen verschiedene Studien, dass ein hohes Alter sowie ein American Society of Anesthesiologists (ASA)-Score von 3 oder mehr Risikofaktoren für die Notwendigkeit einer postoperative intensivmedizinischen Überwachung sind (Bui et al., 2011; Hanak et al., 2014). Dabei scheint das Alter ein umstrittener Risikofaktor zu sein. Unsere Daten zeigen keine Korrelation zwischen dem Alter, einem hohen ASA-Score (>2) und der Notwendigkeit einer postoperativen intensivmedizinischen Überwachung. Ebenfalls zeigt sich die Adipositas als umstrittener Risikofaktor für die Entstehung von postoperativen Komplikationen nach einem neurochirurgischen Eingriff (de Almeida et al., 2018; Ziai et al., 2003). Bezogen auf unserer Daten, konnte die Adipositas (BMI > 30) lediglich nur in der univariaten Analyse als mögliches möglicher Risikofaktor für die Entwicklung einer postoperativen Komplikation beobachtet werden.

Mit dem Fokus auf den intraoperativen Verlauf berichten mehreren Studien, dass ein erhöhter Blutverlust, lange Operationsdauer sowie die Notwendigkeit einer intraoperativen Transfusion von Blutprodukten (Bui et al., 2011; Hanak et al., 2014) mit der Entstehung von postoperativen Komplikationen assoziiert sind. Unsere Daten zeigten jedoch nur den intraoperativen erhöhten Blutverlust von mehr als 325 mL als einen unabhängigen Risikofaktor für die Notwendigkeit einer postoperativen intensivmedizinischen Überwachung.

1.5 Zusammenfassung

Zusammenfassend legen unsere Ergebnisse nahe, dass die Mehrheit der Patienten, die sich einem elektiven resektiven epilepsiechirurgischen Eingriff unterziehen, keine postoperativen Ereignisse entwickeln, welche mandatorisch ein intensivmedizinisches

Setting erfordern. Somit erscheint die postoperative Überwachung dieser Patienten auf einer IMC-Überwachungsstation sicher und machbar. Allerdings sollten Patienten mit Diabetes mellitus und einem erhöhten intraoperativen Blutverlust (>325 mL) weiterhin mit besonderer Umsicht behandelt werden und postoperativ einer intensivmedizinischen Überwachung unterliegen.

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2. Veröffentlichung

JNS

CLINICAL ARTICLE

The necessity for routine intensive care unit admission following elective craniotomy for epilepsy surgery: a retrospective single-center observational study

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OBJECTIVE Traditionally, patients who underwent elective craniotomy for epilepsy surgery are monitored postoperatively in an intensive care unit (ICU) overnight in order to sufficiently respond to potential early postoperative complications. In the present study, the authors investigated the frequency of early postoperative events that entailed ICU monitoring in patients who had undergone elective craniotomy for epilepsy surgery. In a second step, they aimed at identifying pre- and intraoperative risk factors for the development of unfavorable events to distinguish those patients with the need for postoperative ICU monitoring at the earliest possible stage.

METHODS The authors performed a retrospective observational cohort study assessing patients with medically intractable epilepsy (n = 266) who had undergone elective craniotomy for epilepsy surgery between 2012 and 2019 at a tertiary care epilepsy center, excluding those patients who had undergone invasive diagnostic approaches and functional hemispherectomy. Postoperative complications were defined as any unfavorable postoperative surgical and/or anesthesiological event that required further ICU therapy within 48 hours following surgery. A multivariate analysis was performed to reveal preoperatively identifiable risk factors for postoperative adverse events requiring an ICU setting.

RESULTS Thirteen (4.9%) of 266 patients developed early postoperative adverse events that required further postoperative ICU care. The most prevalent event was a return to the operating room because of relevant postoperative intracranial hematoma (5 of 266 patients). Multivariate analysis revealed intraoperative blood loss ≥ 325 ml (OR 6.2, p = 0.012) and diabetes mellitus (OR 9.2, p = 0.029) as risk factors for unfavorable postoperative events requiring ICU therapy.

CONCLUSIONS The present study revealed routinely collectable risk factors that would allow the identification of patients with an elevated risk of postsurgical complications requiring a postoperative ICU stay following epilepsy surgery. These findings may offer guidance for a stepdown unit admission policy following epilepsy surgical interventions after an external validation of the results.

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KEYWORDS elective epilepsy surgery; medically intractable epilepsy; intensive care; healthcare resources

Traditionally, patients who undergo an intracranial neurosurgical approach are admitted to the intensive care unit (ICU) postoperatively, as close monitoring of these patients is considered to be important to identify postoperative complications requiring quick medical or neurosurgical intervention. On the other hand, many studies have shown that only a limited number of patients undergoing elective neurosurgical approaches may require intensive care interventions.[1–3] Furthermore, an appropriate and rapid postoperative transfer of patients to the normal ward seems to be advantageous for patients in terms of accelerating postoperative mobilization and reducing hospital length of stay and, consequently, the risk of hospital-related complications.[4,5] In addition, current limited healthcare resources, most notably ICU capacity and increased costs, demand wise management of this sector.[6,7] Along these lines, many studies have reported significant cost savings through limiting routine ICU ad-

ABBREVIATIONS ASA = American Society of Anesthesiologists; AUC = area under the curve; BP = blood pressure; DM = diabetes mellitus; GCS = Glasgow Coma Scale; ICU = intensive care unit; ROC = receiver operating characteristic.

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mission and implementing standard operating protocols to select those patients who may need ICU interventions postoperatively without threatening patient care.[3–8] However, there is as yet no standardized or consistent policy among neurosurgical departments for selecting the patients with an increased likelihood of developing adverse events requiring an ICU setting after elective craniotomy. In the majority of neurosurgical centers, this decision is based on available resources and individual interdisciplinary evaluation between anesthetists and the neurosurgical team after considering the patient's disease severity and accompanying conditions.

Neurosurgical epilepsy treatment represents a specific kind of elective supratentorial brain surgery involving slightly different patient characteristics, histological diagnoses, and morbidity. Furthermore, developments in epilepsy surgery techniques and neurological monitoring in recent decades have improved the safety of these procedures.[9,10]

We reviewed our institutional database to determine the safety of elective craniotomies for epilepsy surgery and to identify possible pre- and intraoperative risk factors that could predict the necessity for postoperative ICU admission among these patients.

Methods

Patients

All adult patients with medically intractable epilepsy who had undergone elective neurosurgical epilepsy treatment at our institution between 2012 and 2019 were eligible for the study. In order to reduce the heterogeneity of our cohort, the exclusion criteria were as follows: 1) patients who had undergone invasive diagnostic approaches, and 2) patients who had undergone functional hemispherectomy. The medical records of included patients were retrospectively examined and analyzed for this study. Each patient's surgery had been performed on the basis of comprehensive preoperative evaluation, including neurological examination, seizure semiology, long-term video-EEG monitoring, MRI, and invasive diagnostics if necessary. Furthermore, the indication for surgical treatment of these patients with medically intractable epilepsy was given at the interdisciplinary epilepsy surgery conference for every candidate.

We collected and entered into a computerized database (SPSS version 25, IBM Corp.) patient clinical information including age at surgery, sex, type of surgical approach, type of epilepsy (temporal lobe epilepsy vs extratemporal lobe epilepsy), age at epilepsy onset, epilepsy duration, functional status (American Society of Anesthesiologists [ASA] class), relevant accompanying comorbidities and conditions (such as diabetes mellitus [DM], coronary heart disease, hypertension, and obesity), intraoperative duration, estimated blood loss, use of blood transfusions, and surgical abnormalities as well as postoperative adverse events.

Postoperative Standards

After neurosurgical epilepsy treatment, patients are routinely moved to the recovery ward until being discharged to the ICU. During the stay in the recovery ward (1:1:1 patient/anesthesiologist/nurse ratio), the patients are monitored (oxygen saturation, heart rate, noninvasive blood pressure [BP]) and routinely checked for pupillary function, global motor function, and consciousness status.

In the interdisciplinary neurointensive care unit (either 1:3 or 1:2 patient/nurse ratio), the patients are further continuously monitored (oxygen saturation, heart rate, noninvasive BP, and routine blood gas analysis) and neurological examinations are performed by trained nurses on an hourly basis. The ICU course of each patient (including vital parameters, neurological examinations, physician orders, medication records, and event records) was collected and analyzed from either electronic or written inpatient medical records. In addition, all patients undergo MRI within the first 3 days postoperatively in order to determine complete resection of the target structure, in line with previous studies.[11,12] However, postoperative CT scanning is not routinely implemented in an uneventful postoperative course. In the case of a new neurological deficit, immediate CT scanning or even MRI is performed.[13,14]

Identification of Adverse Events

Critical events that required an ICU setting and/or interventions, which are typically not possible on a general neurosurgical ward or stepdown ward, were defined as a Glasgow Coma Scale (GCS) score decrease of more than 2 points, a need to return to the operating room because of clinically relevant postoperative hematoma, a need for reintubation, ischemic stroke, myocardial infarction, the use of intravenous hemodynamic medication, the use of an insulin drip, an ultra-early postoperative seizure, a need for cardiopulmonary resuscitation, and death within the first 48 hours postoperatively.

Statistical Analysis

To interpret the results of this study, data analysis was performed using SPSS Statistics (version 25, IBM Corp.). Fisher's exact test was applied to compare unpaired categorial and binary variables for the two groups, that is, the group needing the ICU and the group that did not. For continuous variables, the Mann-Whitney U-test was performed, as data were mostly not normally distributed (intraoperative duration, estimated blood loss, age at surgery, age at epilepsy onset, and epilepsy duration). The area under the curve (AUC), specificity, and sensitivity, as well as the cutoffs for the significant continuous variables in the Mann-Whitney U-test, were determined using the receiver operating characteristic (ROC) curve to explore the power of the resulting model. Finally, a multivariate analysis was performed to find independent predictors of the need for postoperative ICU admission (using a binary logistic regression analysis), including the variables with significant p values in the univariate analysis. The results of the analysis were presented as odds ratios with 95% confidential intervals. Statistical significance was defined as $p < 0.05$.

Results

Patient Characteristics

Overall, 266 patients (142 [53.4%] male, 124 [46.6%]

TABLE 1. Summary of characteristics of 266 patients who underwent elective craniotomy for epilepsy surgery

Variable	Value
Sex	
M	142 (53.4)
F	124 (46.6)
Mean age at surgery in yrs	37.9 ± 13.4
ASA class	
I	25 (9.4)
II	225 (84.6)
III	16 (6.0)
ICU admission over prior 12 mos	3 (1.1)
BMI in kg/m^2	
<18.5	28 (10.5)
18.5–25	117 (44.0)
25.1–30	74 (27.8)
>30	47 (17.7)
DM	6 (2.3)
Hypertension	33 (12.4)
Mean length of surgery in mins	243 ± 67
Mean intraop blood loss in ml	292 ± 278
Need for intraop blood products	18 (6.8)
Intraop bleeding abnormalities & vulnerable cortex tissue	21 (7.9)

Values are expressed as number (%) or as mean ± standard deviation.

female) with medically intractable epilepsy were surgically treated at our institution between October 2012 and December 2019. The mean age at surgery was 37.9 ± 13.4 years (mean ± standard deviation), and the mean epilepsy duration was 20.5 years. In total, 47 (17.7%) of the 266 patients had a BMI of more than 30 kg/m^2. An ASA class of III was found in 16 (6.0%) of 266 patients. Twenty-five (9.4%) of the 266 patients had undergone a craniotomy of some kind in the past, and 3 (1.1%) of the 266 patients had been admitted to an ICU of some kind in the 12 months prior to our surgery. Further details regarding the baseline patient characteristics are shown in Table 1.

According to intraoperative course documentation, the mean surgery duration was 243 ± 67 minutes and the mean estimated blood loss was 292 ± 278 ml. The operating surgeons described intraoperative bleeding abnormalities in 21 cases (7.9%) as well as vulnerable cortex tissue in their operative reports. A total of 18 patients (6.8%) required transfusion of blood products intraoperatively (Table 1).

Among the 266 patients, 116 (43.6%) underwent transsylvian selective amygdalohippocampectomy. A temporal lobe resection was performed in 34 patients (12.8%), temporal lesionectomy with amygdalohippocampectomy in 22 (8.3%) and without amygdalohippocampectomy in 36 (13.5%), respectively. An extratemporal lesionectomy was performed in 58 patients (21.8%; Fig. 1).

Occurrence of Early Postoperative Adverse Events

Among the entire study population, a total of 13 patients (4.9%) experienced early postoperative adverse events that necessitated an ICU setting. The most common adverse event (5 patients [1.9%]) was the need to return to the operating room because of a clinically relevant postoperative hematoma. Five patients (1.9%) had a significant GCS score decrease of 2 or more points. Intravenous hemodynamic medication was required in 4 patients (1.5%) because of postoperative short-term volume depletion. An ultra-early postoperative focal to bilateral tonic-clonic seizure was observed in 4 patients (1.5%). Clinically relevant strokes within the first 48 hours occurred postoperatively in 2 patients (0.8%), and 2 patients (0.8%) required an in-

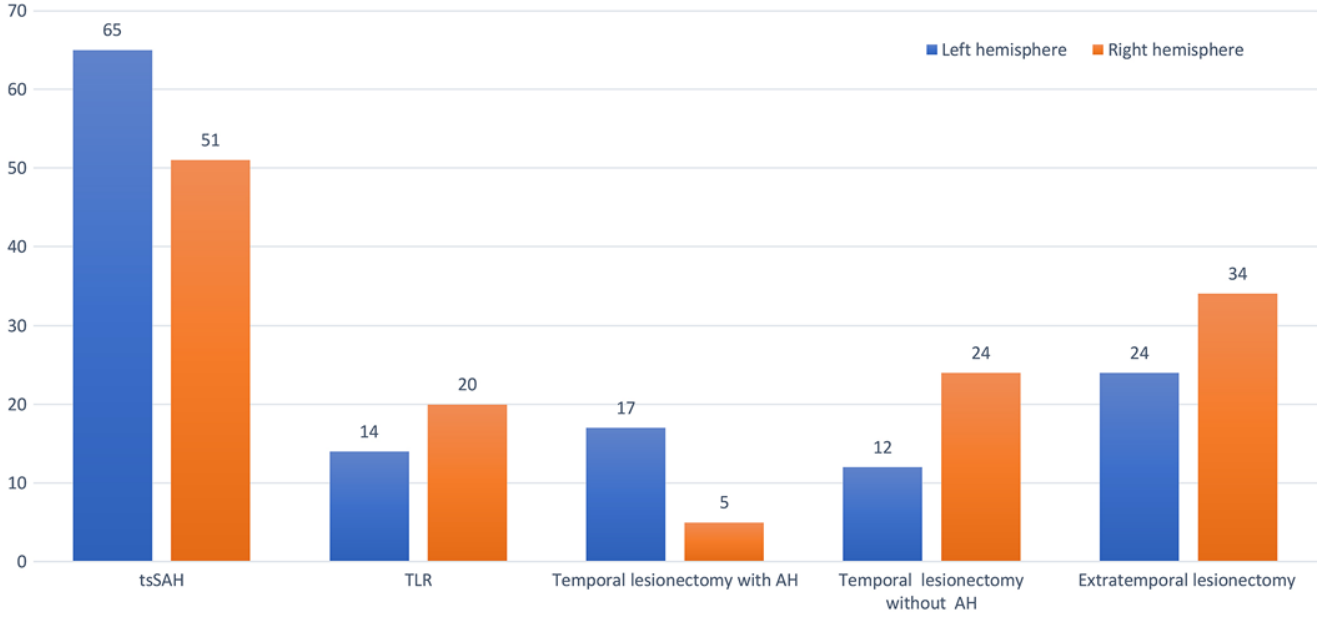

FIG. 1. Diagram showing procedure type and the site at which the procedure was performed. AH = amygdalohippocampectomy; TLR = temporal lobe resection; tsSAH = transsylvian selective amygdalohippocampectomy. Figure is available in color online only.

TABLE 2. Postoperative adverse events requiring ICU care

Measured Outcome	No. of Cases (%)
IV insulin drip	2 (0.8)
IV hemodynamic medication	4 (1.5)
GCS score decrease ≥2 points	5 (1.9)
Ultra-early postop seizure	4 (1.5)
Ischemic stroke	2 (0.8)
Return to OR because of clinically relevant postop hematoma	5 (1.9)

IV = intravenous; OR = operating room.
Some patients experienced more than one significant event necessitating ICU care; therefore, the sum of all significant events is more than the number of the patients needing ICU care.

travenous insulin drip because of severe hyperglycemia (Table 2).

Among the whole cohort, none of the patients died in the hospital, none of them developed myocardial infarction, and none needed cardiopulmonary resuscitation or to be reintubated because of respiratory insufficiency.

Our analysis revealed that 12 (92.3%) of the 13 patients requiring a postoperative ICU setting developed the adverse event within the first 24 hours after surgery. There was only 1 patient (7.7%) out of 13 with a clinically relevant epidural hematoma who required an operative revision more than 24 hours after the initial surgery. For more details, see Fig. 2.

Patient-Related Factors Influencing Postoperative Adverse Events

We found a strong association between early postoperative complications and the patient's comorbidity burden: patients with DM experienced early postoperative adverse events significantly more often than the patients without DM (33.3% vs 4.2%, p = 0.03). In addition, patients with a BMI of more than 30 kg/m^2 were affected by early postoperative unfavorable events significantly more often than those with a BMI of 30 kg/m^2 or less (12.8% vs 3.2%, p = 0.014).

Surgery-Related Factors Influencing Postoperative Adverse Events

In terms of the intraoperative course, patients demonstrated a significant increase in the incidence of postoperative adverse events when the surgeon had reported an intraoperative increased bleeding tendency and vulnerable cortex tissue (p = 0.013). Furthermore, ROC analysis revealed a blood loss cutoff value of 325 ml in terms of the predictability of postoperative adverse events (AUC 0.766, p = 0.001, sensitivity 76.9%, specificity 77.7%). Subsequently, intraoperative blood loss ≥ 325 ml was significantly associated with the prevalence of postoperative adverse events (p < 0.001).

Multivariate Analysis

In order to preoperatively identify patients at high risk for early postoperative complications and therefore the need for postoperative ICU care, we additionally performed a multivariate logistic regression analysis. We found that DM (p = 0.029, OR 9.2, 95% CI 1.26–67.5) as well as intraoperative blood loss ≥ 325 ml (p = 0.012, OR 6.2, 95% CI 1.5–26) was a significant and independent predictor for an increased incidence of postoperative adverse events (Table 3).

Temporal Lobe Epilepsy and Postoperative Adverse Events

In a second step and in an effort to achieve more homogeneity in our cohort, we performed additional statistical analyses of the patients with temporal lobe epilepsy after excluding those with extratemporal lobe epilepsy to identify possible pre- and intraoperative risk factors for the development of postoperative adverse events requiring ICU interventions. The univariate analysis revealed that DM

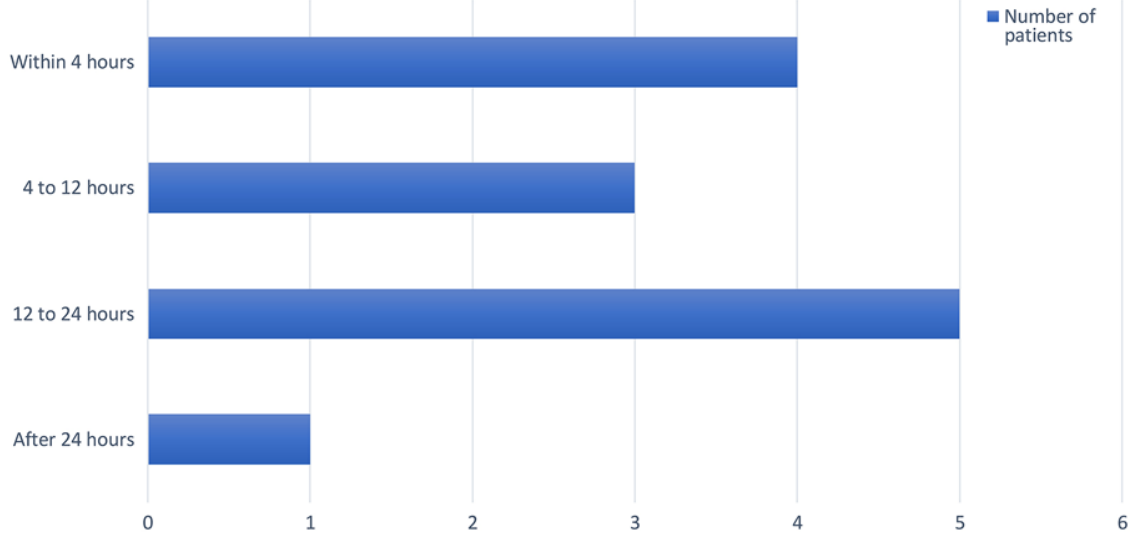

FIG. 2. Time interval between the operation and the adverse event. Figure is available in color online only.

(40% vs 5.4%, p = 0.033) and a BMI of more than 30 kg/m^2 (15.4% vs 4.1%, p = 0.019) were significantly associated with early postoperative unfavorable events. Regarding the intraoperative course, the univariate analysis revealed a significant association between intraoperatively reported increased tissue vulnerability and postoperative unfavorable events requiring ICU intervention (p = 0.025) as well as a correlation between intraoperative blood loss and postoperative unfavorable events (p = 0.001). Furthermore, the multivariate logistic regression analysis identified DM (p = 0.018, OR 12.3, 95% CI 1.54–99) as well as intraoperative blood loss (p = 0.02, OR 5.6, 95% CI 1.35–23.2) as a significant and independent predictor of an increased incidence of postoperative adverse events requiring an ICU setting in patients undergoing temporal lobe epilepsy surgery.

TABLE 3. Multivariate logistic regression analysis of independent predictors of the need for postoperative ICU care

Factor	Adjusted OR	95% CI	p Value
Obesity	2.9	0.83–10.4	0.093
DM	9.2	1.26–67.5	**0.029**
Intraop surgical abnormalities & tissue vulnerability	2	0.3–12.8	0.48
Increased blood loss ≥325 ml	6.2	1.5–26	**0.012**

Boldface type indicates statistical significance (p < 0.05).

Discussion

ICU admission for neurosurgically treated patients is traditionally considered to be necessary at most neurosurgical centers. Along these lines, previous studies have shown that a neuroscience-based ICU may reduce in-hospital mortality in head-injured patients as well as mortality in patients with intracranial hemorrhage.[15,16] Indeed, in patients with good health conditions and fewer comorbidities who undergo elective neurosurgical treatment, recent studies have posited that these patients generally have a good outcome and only a small portion of them may require an ICU setting.[1,17] In line with the statements that elective epilepsy surgery is a low risk approach and that epilepsy patients generally have a good physical condition and fewer comorbidities,[18] our retrospective analysis revealed a 0% in-hospital mortality rate as well as only a 4.9% incidence rate of adverse events necessitating an ICU setting.

Among the 13 patients who required an ICU setting in our cohort, 5 (38.5%) developed an adverse event due to intracranial hematoma. In 4 of them, the symptoms occurred within the first 24 hours after surgery. In only 1 case, the patient developed a convulsive attack due to an epidural hematoma after more than 24 hours after surgery. Interestingly, Taylor et al.[19] could identify two varied intervals in which neurological deficits might occur due to intracranial hematoma after a neurosurgical intervention. The first period occurred within 6 hours and the second after 24 hours following surgery. Basali and colleagues[20] studied the correlation between hypertension and postoperative intracerebral hematoma. In their series, the median occurrence time of neurological deficits due to intracerebral hematoma was 21 hours after surgery. These authors also identified acute intraoperative and early postoperative increased BP values (systolic BP > 160 mm Hg or diastolic BP > 90 mm Hg) as significant risk factors for developing intracranial hematoma. In the series by Hanak et al.,[21] the application of continuous intravenous BP medications in patients with acute increased BP postoperatively was the most frequent ICU intervention (38.75% of their cohort). As the administration of continuous intravenous BP medications at our institution can be also implemented in the intermediate care unit, we did not define it as an ICU intervention in our study. Interestingly, only 21 (7.9%) of the 266 patients in our cohort required continuous intravenous BP medications postoperatively. Four patients (1.5%) required intravenous vasopressors to attain postoperative BP goals (mean arterial pressure ≥ 65 mm Hg). Note that the application of intravenous insulin drips and catecholamines with the necessary monitoring is permitted only in our ICU. In our cohort, only 2 patients needed intravenous insulin drip postoperatively because of postoperative hyperglycemia, defined as a blood glucose level higher than 160 mg/dl, and the consideration of the neuroprotective effect of normoglycemia in neurocritical care.[22,23] Both patients had preoperatively known DM.

In terms of pre- and intraoperative risk factors, Hanak et al.[21] assessed 400 patients who had undergone elective craniotomy with regard to postoperative ICU intervention and identified DM and older age as independent predictors of postoperative adverse events. In the current series, the multivariate analysis also yielded DM as an independent risk factor. In another study, older age was also a predictive risk factor for postoperative adverse events in a cohort of 343 patients undergoing elective craniotomy, as reported by Bui and colleagues.[1] However, older age as a risk factor seems to be controversial, as other studies have failed to find such a correlation.[24,25] In the current series, age at surgery did not correlate with a higher prevalence of postoperative adverse events. Moreover, the mean age of our cohort was 37.9 ± 13.4 years and is distinctly lower than the reported ages in the aforementioned studies. In terms of BMI, many studies have reported that obese patients have higher readmission rates as well as higher risks of reoperation for infection after elective craniotomy for tumor.[26,27] Likewise, Dasenbrock et al.,[28] in a National Surgical Quality Improvement Program analysis, reported increased odds for major perioperative complications in obese patients after craniotomy for tumor. The ASA classification scheme is used worldwide for preoperative patient assessments. Hanak et al.[21] described a significant increased prevalence of postoperative adverse events in patients with an ASA class ≥ III. Furthermore, in a multivariate analysis, they identified intraoperative blood products transfusion as a predictive risk factor (in addition to DM and higher age). However, in the current study, we could not confirm the higher ASA class, obesity, and intraoperative blood products transfusion as independent risk factors. Furthermore, and in line with their results, our analysis showed that the performed surgical procedure did not correlate with the prevalence of postoperative adverse events. Moreover, given the nature of our cohort, type of epilepsy (temporal lobe epilepsy vs extratemporal lobe epilepsy) was not associated with a higher prevalence of

postoperative adverse events. Likewise, the second logistic regression analysis of patients with temporal lobe epilepsy yielded the same independent risk factors regarding early postoperative adverse events necessitating ICU settings.

Interestingly, our univariate analysis revealed intraoperatively reported increased tissue vulnerability as a possible risk factor for the need of an ICU setting postoperatively. This finding led us to further investigation; given the elective nature of the studied cases and considering the standardized surgical approaches implemented by several certified epilepsy neurosurgeons at our institution, all patients were routinely examined for coagulopathy (international normalized ratio, partial thromboplastin time, fibrinogen level in blood serum as well as fibrin stabilizing factor). Patients with known antiplatelet or anticoagulant medication were asked to discontinue the intake of these medications for an appropriate period preoperatively. After that, to rule out any residual effect of these medications, an appropriate preoperative laboratory study was performed. None of the reported cases of intraoperative bleeding abnormalities had perceptible preoperative coagulopathy. Furthermore, in all 21 cases, comprehensive intraoperative laboratory studies were performed to investigate for potential coagulopathy. According to the results, blood products and exhausted coagulation factors were substituted. Intriguingly, 15 (71.4%) of the 21 reported cases had a postoperative histologically confirmed diagnosis of hippocampal sclerosis. This aspect led us to search the literature for potential coherence; unfortunately, we could not find a distinct connection between the two points. However, according to our research, it can be assumed that the presumed immunological and inflammatory response in patients with mesial temporal lobe epilepsy with hippocampal sclerosis could play a role in modifying the cortex tissue, which seemed to be vulnerable intraoperatively.[29–31] However, an additional analysis of patients with histologically confirmed hippocampal sclerosis using Fisher's exact test did not reveal a significant correlation with an increased risk of developing a postoperative adverse event requiring an ICU setting ($p = 0.059$). Furthermore, the multivariate analysis did not reveal the intraoperatively described increased tissue vulnerability as an independent risk factor.

Our findings regarding elective craniotomy for epilepsy surgery are consistent with the practice of not routinely admitting to the ICU those patients undergoing elective supratentorial craniotomy unless certain preoperative and intraoperative conditions are present. In addition, considering the noted postoperative adverse events, we can state that the ICU setting in our cohort was required, in particular, for close neurological monitoring and intravenous medication drips. Therefore, we suggest that patients undergoing elective craniotomy for epilepsy surgery do not typically require the full capability of ICU resources and that a stepdown unit with a focus on neurological and physical surveillance and rapid response rates could be safe for monitoring these patients postoperatively. However, this conclusion is underpowered because of the study design and the fact that there are intangible factors of ICU settings that could not be quantified or assessed in this study. Hence, we recommend a multicenter prospective trial addressing the external validation of our results to establish a valid algorithm for admitting patients to the ICU after neurosurgical epilepsy treatment solely in cases of relevant comorbidities or intraoperative abnormalities.

Study Strengths and Limitations

Without doubt, the present study has certain limitations. As with all retrospective studies, the limitations of our study are inherent in its design and include retrospective data collection from a single center. Furthermore, we acknowledge that the variability in the surgical caseload, nursing staff numbers, and skill set between our institution and others will definitely have an impact on the applicability of these results to any particular institution. Therefore, external validation of our results is indispensable. Moreover, there was no quality of life assessment due to the overnight admission to the ICU to survey patient satisfaction, nor any cost-benefit analysis, which may exhibit a possible cost savings. An additional shortcoming due to the retrospective nature of our data without a control group was the inability to draw conclusions regarding whether adverse events could be detected early enough in a patient who had been admitted to a stepdown unit postoperatively. Therefore, we encourage further studies with a prospective and controlled design addressing this issue. Additionally, the reported risk factor of increased tissue vulnerability intraoperatively is rather an objective assessment and inherent in the experience of the neurosurgeon and should be interpreted with care.

On the other hand, the strengths of the present study are its narrowly defined cohort, which reduces the heterogeneity of the study population and may eliminate possible confounders. Moreover, the large sample size in relation to the number of studied potential risk factors is another particular strength, which may increase the reliability of our multifactorial logistic analysis. In addition, our standardized surgical approaches, implemented by only a few neurosurgeons, may reduce possible confounding factors caused by distinctions in surgical practice. All of these factors provide good warrants about the internal validity of our study.

Conclusions

The present study reveals routinely collectable factors that allow the identification of patients with an elevated risk of postsurgical complications requiring a postoperative ICU stay following epilepsy surgery. These findings may offer guidance for a stepdown unit admission policy following epilepsy surgical interventions. However, attention should be paid to patients with increased intraoperative blood loss (≥ 325 ml) and DM, who should be monitored postoperatively in the ICU. To confirm our results and to survey the external validation of how a selective postoperative ICU admission could be safe after elective surgical epilepsy treatment, further multicenter prospective studies must be performed.

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Disclosures

Dr. Rácz has received honoraria from UCB Pharma. Dr. Surges is part of the speakers bureaus for Arvelle, Bial, Desitin, Eisai, Livanova, Novartis, and UCB Pharma and is a consultant for Arvelle, Bial, Eisai, Livanova, UCB Pharma, and UNEEG.

Author Contributions

Conception and design: Bahna, Vatter, Borger. Acquisition of data: Bahna. Analysis and interpretation of data: Bahna, Borger. Drafting the article: Bahna. Critically revising the article: Bahna, Schneider, Borger. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Bahna. Statistical analysis: Bahna, Borger. Administrative/technical/material support: Bahna, Schneider, Borger. Study supervision: Vatter, Borger.

Supplemental Information

Previous Presentations

Parts of this work were presented as an oral presentation at the 72nd Annual Meeting of the German Society of Neurosurgery (DGNC) held in Erfurt, Germany, on June 6–9, 2021.

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