








FULL-LENGTH ORIGINAL RESEARCH

Classification of complications of epilepsy surgery and invasive diagnostic procedures: A proposed protocol and feasibility study

Johan Bjellvi^{1,2}  | J. Helen Cross^{3,4,5}  | Maria Gogou⁴ | Mathilde Leclercq⁶ | Sylvain Rheims⁶  | Philippe Ryvlin⁷  | Michael R. Sperling⁸  | Bertil Rydenhag^{1,9}  | Kristina Malmgren^{1,2} 

¹Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

²Department of Neurology, Sahlgrenska University Hospital, Member of the ERN EpiCARE, Gothenburg, Sweden

³UCL-NIHR BRC Great Ormond Street Institute of Child Health, London, UK

⁴Great Ormond Street Hospital for Children, Member of the ERN EpiCARE, London, UK

⁵Young Epilepsy, Lingfield, UK

⁶Department of Functional Neurology and Epileptology, Hospices Civils de Lyon and Lyon 1 University, Member of the ERN EpiCARE, Lyon, France

⁷Department of Clinical Neurosciences, CHUV, Lausanne, Switzerland

⁸Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA

⁹Department of Neurosurgery, Sahlgrenska University Hospital, Member of the ERN EpiCARE, Gothenburg, Sweden

Correspondence

Johan Bjellvi, Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Blå stråket 7, 413 45 Göteborg, Sweden.

Email: johan.bjellvi@vgregion.se

Funding information

National Institute of Health Research (NIHR) Biomedical Research Centre at Great Ormond Street Hospital; Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement, Grant/Award Number: ALFGBG-517901 and ALFGBG-723151

Abstract

Objective: In epilepsy surgery, which aims to treat seizures and thereby to improve the lives of persons with drug-resistant epilepsy, the chances of attaining seizure relief must be carefully weighed against the risks of complications and expected adverse events. The interpretation of data regarding complications of epilepsy surgery and invasive diagnostic procedures is hampered by a lack of uniform definitions and method of data collection.

Methods: Based on a review of previous definitions and classifications of complications, we developed a proposal for a new classification. This proposal was then subject to revisions after expert opinion within E-epilepsy, an EU-funded European pilot network of reference centers in refractory epilepsy and epilepsy surgery, later incorporated into the ERN (European Reference Network) EpiCARE. This version was discussed with recognized experts, and a final protocol was agreed to after further revision. The final protocol was evaluated in practical use over 1 year in three of the participating centers. One hundred seventy-four consecutive procedures were included with 35 reported complications.

Bertil Rydenhag and Kristina Malmgren contributed equally to the supervision of the manuscript.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2021 The Authors. *Epilepsia* published by Wiley Periodicals LLC on behalf of International League Against Epilepsy.

Results: This report presents a multidimensional classification of complications in epilepsy surgery and invasive diagnostic procedures, where complications are characterized in terms of their immediate effects, resulting permanent symptoms, and consequences on activities of daily living.

Significance: We propose that the protocol will be helpful in the work to promote safety in epilepsy surgery and for future studies designed to identify risk factors for complications. Further work is needed to address the reporting of outcomes as regards neuropsychological function, activities of daily living, and quality of life.

KEYWORDS

adverse effects, adverse events, intracranial EEG, invasive EEG, Wada test

1 | INTRODUCTION

Balancing the risks and benefits may be demanding in epilepsy surgery, which irrevocably alters targeted brain networks with the ultimate aim of improving quality of life as well as reversing the morbidity and disabilities associated with epilepsy. Monitoring adverse effects is essential for quality control and for counseling patients, families, and caregivers before surgery. Ideally, data on adverse effects should be obtained in a standardized and reproducible manner to allow comparisons between different surgical procedures and centers. Prospective data collection reduces the chances of selective reporting. As highlighted in several reviews, published rates of adverse effects in epilepsy surgery vary markedly, in part due to differences in definitions and data collection.¹⁻⁴

The Clavien-Dindo classification of complications (1992/2004) has been used widely in many fields of surgery, defining complications as any deviation from the normal postoperative course. Complications are graded based on the interventions needed to correct their effects, and a suffix may indicate whether the patient has a complication at the time of discharge.⁵⁻⁷ As of today, this classification has not been used in studies of epilepsy surgery.

For general neurosurgery, a similar system has been proposed by Landriel Ibañez et al.⁸ Here, complications are graded based on the invasiveness of the measures needed to reverse the complication. A suffix indicates whether any new neurological deficit improves within 30 days of the surgical procedure. Houkin et al.⁹ classify adverse effects in terms of predictability and avoidability, and in a recent proposal, neurosurgical complications are classified based on their hypothesized cause.¹⁰

In epilepsy surgery, several authors have classified complications as transient vs permanent, or minor vs major, based on whether any neurological deficits persist beyond a certain time of follow-up, such as 1 year or 3 months.^{11,12} Other authors have graded complications

Key Points

- Multicenter studies with uniform protocols are necessary for studying the complications of epilepsy surgery and invasive diagnostic procedures
- Previous definitions and classifications are reviewed
- A multidimensional protocol for reporting complications is proposed
- Complications are registered in terms of immediate consequences, permanent symptoms, and consequences of permanent disability on activities of daily living

based on both the need for intervention and the permanence of neurological deficits, and if invasive monitoring had to be aborted prematurely.¹³⁻¹⁵ Further classifications have taken into account whether the hospital stay was prolonged and whether the Glasgow Coma Scale score was affected.¹⁶ A recent study applied the four-graded classification of Landriel Ibañez et al. in parallel with the dichotomy of transient vs permanent morbidity.¹⁷

As seen, complications in epilepsy surgery can be graded based on direct patient-related factors, such as persistence of neurological morbidity, or based on procedure-related factors, such as revision of planned monitoring and hospital stay. An alternative to a single severity scale, which so far has not been implemented in epilepsy surgery, is a multidimensional classification protocol, where several of these factors are taken into account.

The rate of complications will be influenced by how they are defined. Some reports of adverse events of epilepsy surgery and diagnostic procedures regard any untoward event during the postoperative course as a complication, whereas others exclude certain types of

neurological worsening, if judged as expected, and considered an acceptable trade-off in preoperative counseling.

Previous studies have identified a number of risk factors for complications, for example, increased number of electrodes in invasive monitoring^{1,18,19} and older age at the time of the operation in epilepsy surgery.^{13,20–22} The limited number of cases with adverse events identified in each center hampers the relevance or robustness of statistical analysis. A Swedish population-based study reported an association between complications related to invasive monitoring and complications in subsequent epilepsy surgery. Due to the small number of cases, the potential causes for this association remained elusive.²³ To include the number of patients necessary for exploring such associations, larger multicenter studies with uniform protocols are needed.

The primary aim of this report was to propose an evidence-based protocol for prospective registering of complications in invasive diagnostic procedures and epilepsy surgery, which will be useful in future studies identifying risk factors for complications. In the proposed protocol, only unexpected adverse events are regarded as complications. A secondary aim was to evaluate the usefulness of this protocol in a feasibility study.

2 | METHODS

2.1 | Literature search

In order to review previous definitions and classifications of complications, we conducted a literature search in PubMed, Scopus, and Cochrane Library for articles published up to January 1, 2017, with the term “epilepsy surgery” and “adverse effect*”, “adverse event*”, or “complication*” in the title and/or abstract. As there are no MeSH terms for invasive investigations,¹ we conducted a test search including various terms for specific invasive investigations (such as “intracranial EEG”, “SEEG”, and “Wada test”) without significant numbers of additional results.

Original publications and systematic reviews regarding epilepsy surgery and invasive diagnostic procedures with populations >30 were eligible for review in full text if complications or other adverse events were reported as indicated in the abstract. Studies reporting only neuropsychological and psychiatric adverse events were excluded, as were studies reporting only adverse events related to neurostimulation procedures. We compiled definitions and classifications encountered when reviewing the full text and searched the relevant articles for further citations. Major reviews were searched for additional references.^{1–3,24}

2.2 | Preparation of the protocol and reaching consensus

We propose a multidimensional protocol for reporting complications, where the consequences of complications are registered in terms of their immediate consequences, resulting permanent symptoms, if any, and the consequences of permanent disability on activities of daily living.

The protocol addresses complications related to invasive diagnostic procedures, including the Wada test and invasive electroencephalography (EEG) monitoring procedures, and epilepsy surgery. Adverse effects, which are also seen in noninvasive seizure monitoring—for instance, falls, fractures, status epilepticus, and psychiatric disorders—will require separate registration.^{25,26} Neurostimulation procedures are not addressed in this protocol.^{27,28}

The protocol was designed as follows. Based on the literature search, previously used classifications of complications in epilepsy surgery and known risk factors for complications were reviewed to identify relevant items to include in the protocol.

Three of the authors (JB, BR, and KM) prepared a first version of the protocol. This was presented to the European consortium of epilepsy surgery centers within the EU-funded project E-epilepsy, a European pilot network of reference centers in refractory epilepsy and epilepsy surgery, later incorporated into the ERN EpiCARE (<https://epicare.eu/therapeutics/8-surgery-e-epilepsy/>). After a revision based on expert opinion from the E-epilepsy consortium, the proposed classification has been further discussed by the International League Against Epilepsy (ILAE) Commission on Surgical Therapies and the ILAE Task Force on Pediatric Epilepsy Surgery 2013–2017. A final version was agreed to by members of the E-epilepsy consortium.

2.3 | Feasibility study

To evaluate the functionality of the protocol, three of the centers (Great Ormond Street Hospital for Children, Hospices Civils de Lyon, and the Sahlgrenska University Hospital) agreed to participate in a feasibility study. All patients who underwent epilepsy surgery or invasive diagnostic procedures at the participating centers during a 1-year evaluation period were consecutively included. In accordance with the protocol, the patients were evaluated for complications and neurological function at the time of surgery and 6 months after surgery. Only unexpected adverse events were reported as complications according to the definition in the protocol (see below). Anonymized forms were sent to one of the authors (JB) for compilation

and analysis. The regional boards of ethics of each center considered this activity as a quality control measure that did not require individual consent.

3 | RESULTS

3.1 | Literature review

After removing duplicates, the initial literature search rendered 3953 results, from which 304 articles were obtained and reviewed in full text. Of these, 125 articles were found where a definition (68 articles) and/or classification (107 articles) was stated in the Methods or Results section. The definitions and classifications found are summarized in Appendix S1.

3.2 | Protocol

Separate protocols are proposed for invasive diagnostic procedures and for epilepsy surgery. The headings are listed in Table 1 for invasive diagnostic procedures and Table 2 for epilepsy surgery, whereas all items can be seen in Appendices S2 and S3, respectively. The protocol can be integrated in each center's follow-up database, which provides access to basic demographic data, and allows it to elucidate relationships if complications occur during invasive monitoring and surgery in the same patient.

Following previous reports, complications are defined as unwanted, unexpected, and uncommon events directly related to an invasive diagnostic procedure, surgical resection, or disconnection.

Complications are reported in a step-by-step fashion as follows.

3.3 | Complications related to invasive diagnostic procedures

1. For invasive diagnostic procedures (Wada test and invasive EEG monitoring), the protocol requires a detailed characterization of the performed procedure, including number, type, and localization of electrode contacts, when relevant, and the duration of monitoring. For instance, the use of subdural grids has been shown to carry an increased risk for complications compared to subdural strips and depth electrodes,^{23,29} which increases with longer duration of monitoring,³⁰ larger number of electrodes,^{1,18,19} and size of subdural grids.³¹
2. It is specified whether prophylactic antibiotics and/or medical venous thromboembolism (VTE) prophylaxis are given. It has been suggested that the duration

TABLE 1 Proposed classification of complications related to invasive diagnostic procedures

1. Specify invasive diagnostic procedure
 - 1.1. Wada test
 - 1.2. Invasive monitoring procedures (specify number of monitoring days and number and localization of electrode contacts)
 - 1.2.1. Subdural grids
 - 1.2.2. Subdural strips
 - 1.2.3. Foramen ovale electrodes
 - 1.2.4. Depth electrodes (excluding stereo-EEG)
 - 1.2.5. Stereo-EEG
2. Prophylactic medication
 - 2.1. Antibiotics
 - 2.2. VTE prophylaxis
3. Complications
 - 3.1. Surgical complications
 - 3.2. Acute medical complications requiring intervention
 - 3.3. Neurological deficits (only new, unexpected deficits or unexpected significant worsening of preoperative deficits) and other major unexpected symptoms
4. Impact of perioperative complications (additional unplanned surgical intervention, unplanned readmission or prolongation of existing hospitalization, potentially life-threatening complication, death, if any of the above)
5. Permanent symptoms (only new, unexpected neurological deficits or unexpected significant worsening of preoperative deficits persisting at 6 months postoperatively, or major unexpected symptoms, such as cosmetic deficits)
6. Consequences of permanent neurological deficits on dependency and activities of daily living

of prophylactic antibiotic treatment may influence the risk of infective complications in invasive monitoring,³² although this has been questioned in other studies.^{33,34} The role of VTE prophylaxis in invasive monitoring and epilepsy surgery has been insufficiently studied. According to a recent review, controversy remains as to whether the efficacy of VTE prophylaxis outweighs the risk of hemorrhage in patients who undergo craniotomy for brain tumor resection.³⁵ Because invasive monitoring necessarily involves a certain degree of immobilization, we judged it important to assess the possible influence of VTE prophylaxis. Up to this point, the details of the procedure are reported identically whether a complication occurs or not, in order to provide adequate controls for cases with complications.

3. Complications are affirmed or denied in a multiple-choice fashion. The potential complications are, for clarity, divided into surgical complications and acute medical complications. The choice of complications is based on previous reviews to include the most common

TABLE 2 Proposed classification of complications related to epilepsy surgery

1. Location of resection/lesionectomy, or specify disconnection
1.1. Resection/lesionectomy
1.2. Hemispheric procedure
1.3. Callosotomy
1.4. Other
2. Prophylactic medication
2.1. Antibiotics
2.2. VTE prophylaxis
3. Complications
3.1. Surgical complications
3.2. Acute medical complications requiring intervention
3.3. Neurological deficits (only new, unexpected deficits or unexpected significant worsening of preoperative deficits) and other major unexpected symptoms
4. Impact of perioperative complications (additional unplanned surgical intervention, unplanned readmission or prolongation of existing hospitalization, potentially life-threatening complication, death, if any of the above)
5. Permanent symptoms (only new, unexpected neurological deficits or unexpected significant worsening of preoperative deficits persisting at 6 months postoperatively, or major unexpected symptoms, such as cosmetic deficits)
6. Consequences of permanent symptoms on dependency and activities of daily living

and serious complications.^{1,3,20,23} Any unlisted complication, for instance, any of the adverse effects that are specifically related to the Wada test^{36–38} or postoperative headache of unexpected nature or intensity,³⁹ can be specified. Several complications can be chosen for each patient, if relevant. If no complication occurs, the reporting process stops here.

- Any neurological deficits during the perioperative period are reported. Following the definition, only new, unexpected deficits or unexpected significant worsening of preoperative deficits are noted. Deficits are listed as major groups as in previous reports.^{1–3,11,12,20} The protocol adds a new item, that is, major cosmetic deficit, being an outcome of potential importance for the patient's quality of life. Furthermore, it is possible to specify any deficit that is not reported appropriately under the major headings. As will be discussed later, cognitive sequelae are not included.
- The impact of complications is characterized in terms of whether they result in any additional unplanned surgical procedures, unplanned readmission or prolongation of hospital stay, or death, or if they are life-threatening; or none of the above. The choice of factors was made to include the major items used in previous classifications.^{6–9,14,16}

- Any permanent neurological morbidity is described in terms of new, unexpected deficits or unexpected significant worsening of preexisting deficits (as noted above for the perioperative period), which persist 6 months after surgery. Persistent major cosmetic deficits are also reported at this point. The 6-month limit proposed here was reached by consensus, as recovery is mostly complete beyond this time.
- The consequences of permanent morbidity on activities of daily living and dependency are reported. This important aspect of complications has not been taken into account in previous reports in epilepsy surgery or invasive diagnostic procedures. We agreed to use the modified Rankin Scale (mRS), which has been used and validated in several neurological and neurosurgical conditions.^{40,41}

3.4 | Complications related to epilepsy surgery

For epilepsy surgery procedures (resective and disconnective), the type and localization of the procedure are reported in the first step. Commonly performed types of epilepsy surgery are listed in the protocol.⁴² Very rare procedures, such as multiple subpial transections, are registered as “other” and specified manually.

This is followed by specifying surgical and acute medical complications, perioperative neurological deficits, impact of complications, permanent morbidity, and consequences of permanent morbidity, in the same manner as for invasive diagnostic procedures.

3.5 | Feasibility study

During the inclusion period, 174 procedures were performed. Of these, 53 were invasive diagnostic procedures (52 stereo-EEG (SEEG) procedures and one exploration with grid and depth electrodes) and 121 epilepsy surgery procedures (36 temporal resections, 30 frontal resections, 14 hemispherotomies, 9 parietal resections, 7 complete callosotomies, 6 multilobar resections, 6 multilobar disconnections, 4 hypothalamic hamartoma procedures, 2 insular resections, 2 thermocoagulations, and 5 other procedures). Ninety-six (55%) of the patients were male. Patients' ages ranged from 11 months to 54 years (mean 18 years). Forty-eight (28%) of the patients had a previous neurological deficit. Twenty-seven (16%) had previous intracranial surgery (18 epilepsy surgery, 6 invasive EEG, 2 both, and one other). Duration of invasive registrations was 3–17 days (mean 10 days).

Following the definition in the protocol, only unexpected adverse events were reported as complications. In

total, 35 patients (20%) had complications, which were related to 5 of the 53 invasive diagnostic procedures (9%, all SEEG), and 30 of the 121 epilepsy surgery procedures (25%) (Table 3). Eight complications had an impact on the postoperative course: (1) in SEEG implantations, management of a superficial wound infection in one case and electrode removal in two cases; (2) in epilepsy surgery, unplanned readmission or prolongation of hospital stay in three cases, bone flap removal in one case, and readmission to intensive care due to a life-threatening complication in one case.

In nine cases (5.2% of all procedures), one SEEG implantation and eight resections, symptoms persisted 6 months after the procedure. These symptoms were a mild sensory disturbance after SEEG implantation, diabetes insipidus after a hypothalamic hamartoma resection, partial sensory loss after two parietal resections, dysesthesia after an insular resection, diplopia after an anterior temporal lobe resection, dysnomia after an anterior temporal lobe resection, reading difficulties after a parieto-occipital resection, and reading difficulties and disabling vertigo after a temporo-occipito-basal resection. Two patients, one of whom had a perioperative complication, did not have follow-up at 6 months because they lived abroad.

The reporting was complete for most items with the following exceptions. For many SEEG implantations, the number of electrode contacts or number of monitoring days was lacking. Some participating centers reported this information to be not easily available. In some cases, it was not reported whether VTE prophylaxis was given, but this could be clarified by contacting the center. Outcome according to the mRS was not specified for 2 of the 35 cases with complications.

4 | DISCUSSION

The main advantage of the proposed protocol is its comprehensive coverage of patient- and procedure-related factors, which are relevant to the identification of risk factors for complications. In an internet-based setting, data could easily be retrieved for further analysis and applied for different purposes. No existing severity scale has been incorporated into the protocol, but the information for such stratification can be extracted. For instance, classification of complications into major symptoms (symptoms persisting after 6 months) and minor symptoms (symptoms resolving within 6 months) could easily be performed based on the database, as well as classification accounting for the need for interventions.

The number of items in the proposed protocol may appear demanding. However, as judged from our feasibility study, detailed reporting of complications according to the

protocol is possible if performed routinely in a center. For the majority of patients who do not have any complications, only the nature of the procedure has to be reported and the occurrence of complications negated. For patients who have a complication, with or without persistent morbidity, detailed background information on the procedure performed and the nature of the complication is needed for informative analysis. For instance, a number of studies on invasive monitoring lack information on the number of electrodes and the duration of monitoring that have been associated with an increased risk for complications.¹

4.1 | Definitions

It is important to note that in the present protocol, only new and unexpected neurological deficits or significant unexpected worsening of preoperative deficits are reported as complications. The Swedish National Epilepsy Surgery Register defines a complication as an “unwanted, unexpected, and uncommon event after a diagnostic or therapeutic procedure.”^{12,20} Similarly, Behrens et al.¹¹ stated that short-lasting and reversible deficits that occurred after surgery in the immediate vicinity of functionally important brain areas were not regarded as complications, nor were persistent deficits, which were judged to be inevitable and discussed with the patient prior to surgery, for example, hemianopia after occipital lobe resection.

Conversely, when prospectively monitoring complications in pediatric invasive investigations, Blauwblomme et al.¹⁶ followed a previous definition of a complication as “any untoward event related to a child’s admission which had the potential to increase their stay in hospital and/or produce a temporary or permanent worsening of their health.”⁴³ Such a definition will be more inclusive compared to when expected adverse events are not reported. In invasive EEG investigations, small, asymptomatic hemorrhages are common and the rate of this complication will depend on whether these are reported.^{44–46}

Clavien et al. defined three types of negative outcome in surgery: complications, sequelae, and failures of surgical therapy. Sequelae were defined as alterations in body function that are inherent to the nature of the procedure, whereas failures indicate that the purpose of the procedure is not fulfilled, that is, recurrence of a tumor.⁶

In epilepsy surgery, failure of surgery would often amount to lack of worthwhile seizure reduction, depending on the preoperative goal. Obvious examples of sequelae are, as in any type of surgery, scars and a certain amount of postoperative pain. We also believe that in epilepsy surgery, some neurological deficits are very common and should be regarded as inherent to the procedure, and hence as sequelae. For instance, loss of useful hand

TABLE 3 Complications reported in a 1-year feasibility study

Case no.	Procedure	Perioperative complications	Impact/intervention	Permanent symptoms	mRS
1	SEEG	Asymptomatic subdural hematoma seen on MRI after electrode removal; superficial wound infection	Yes (management of superficial wound infection)	No	0
2	SEEG	Incarceration of intracerebral electrode	Yes (electrode removal)	No	0
3	SEEG	Patient pulled out electrodes during confusional awakening	Yes (electrode removal)	No	0
4	SEEG	Transient sensory disturbance of the upper left limb	No	No	0
5	SEEG	Discrete sensory disturbance of two fingers in the right hand	No	Yes (sensory disturbance)	2
6	Anterior temporal resection	Diplopia noted 3 months after surgery, improved after 6 months	No	Yes (diplopia)	-
7	Anterior temporal resection	Dysnomia without difficulties of comprehension noted 3 months after surgery, improved after 6 months	No	Yes (dysphasia)	-
8	Anterior temporal resection	Subdural hematoma	Yes (unplanned readmission/prolongation of hospital stay)	No	0
9	Anterior temporal resection	Subdural hematoma	Yes (unplanned readmission/prolongation of hospital stay)	No	0
10	Anterior temporal resection	Readmission because of severe headache	Yes (unplanned readmission/prolongation of hospital stay)	No	0
11	Other temporal (temporo-occipitobasal lesionectomy)	Reading difficulties and vertigo which improved over 6 months	No	Yes (reading difficulties and vertigo)	2
12	Frontal lesionectomy	Infection with required sacrificing the bone flap	Yes (bone flap removal; management of superficial wound infection; unplanned readmission/prolongation of hospital stay)	No	0
13	Frontal lesionectomy	Fever of unknown cause, oral and vaginal candidiasis	No	No	0
14	Frontal lesionectomy	Facial weakness	No	No	0
15	Frontal lesionectomy	Mild hemiparesis which improved quickly	No	No	0
16	Frontal lesionectomy	Hemiparesis affecting lower more than upper limb	No	No	0
17	Frontal lesionectomy	Right arm weakness with full recovery after exercises	No	No	0
18	Frontal lesionectomy	Discrete paresis of upper left limb which resolved within a few days	No	No	0

(Continues)

TABLE 3 (Continued)

Case no.	Procedure	Perioperative complications	Impact/intervention	Permanent symptoms	mRS
19	Frontal parenchymal resection	Right arm weakness	No	No	0
20	Frontal parenchymal resection	Transient hemiparesis and aphasia	No	No	0
21	Frontal parenchymal resection	Intraparenchymal hematoma	No	No	0
22	Insular lesionectomy	Dyesthesia involving both hands	No	Yes (sensory disturbance)	1
23	Parietal lesionectomy	No perioperative complication noted	No	Yes (partial sensory loss)	1
24	Parietal parenchymal resection	Weakness left leg and foot with resolved within a few days and persisting sensory disturbance in the same area	No	Yes (sensory disturbance)	3
25	Opercular-parietal parenchymal resection	Transient facial weakness which resolved prior to discharge	No	No	0
26	Temporal and parietal disconnection	Headache and photophobia	No	No	0
27	Temporo-parieto-occipital disconnection	Mild hemiparesis	No	No	0
28	Hemispherotomy	Addisonian crisis	Readmission to intensive care, life-threatening complication	No	3
29	Hemispherotomy	Addisonian crisis	No	No	1
30	Hemispherotomy	Thrombosis in deep cerebral veins and vein of Galen	No	No	0
31	Hemispherotomy	Postoperative pyrexia which required intravenous treatment	No	No	0
32	Hemispherotomy	Diabetes insipidus requiring treatment with desmopressin	No	No	0
33	Callosotomy	Skin rash	No	No	0
34	Hypothalamic hamartoma resection	Metabolic derangement requiring desmopressin and fluid treatment	No	Yes (diabetes insipidus)	1
35	Hypothalamic hamartoma resection	Brief stridor following extubation	No	No	0

function is an expected consequence of hemispheric surgery, which will be discussed preoperatively and, in some cases, lead to the decision to perform a more limited resection.^{47,48} Similarly, minor visual field deficits occur in 48%–100% of patients who undergo temporal lobe surgery for epilepsy, and most of them are asymptomatic. On the other hand, major visual field defects occur in a minority of patients, with impact on daily function, quality of life, and eligibility to drive.⁴⁹ Consequently, some minor visual field deficits should be regarded as expected adverse effects in the context of temporal lobe surgery, whereas hemianopia is to be counted as a complication.

Over time, the introduction of new techniques in surgery and radiology may reduce the rate of visual field defects.^{49,50} In general, the rate of complications in epilepsy surgery has decreased dramatically over 30 years.²⁴ We, therefore, acknowledge a certain degree of subjectivity regarding what is to be expected from epilepsy surgery in terms of neurological worsening or other adverse events. In borderline cases, we suggest that the event should be reported as a complication.⁶

Although the feasibility study was designed to assess the functionality of the protocol, we note that rates of complication (9% for SEEG and 25% for epilepsy surgery) were higher compared to other studies with similar definitions and prospective data collection.^{12,20} In a limited sample, the types of surgical procedures and characteristics of the patient cohort (such as a high proportion of hemispheric surgeries and young patients with preoperative deficits) are likely to influence the results. We also believe that the multi-dimensional nature of the present proposal may encourage centers to report “minor” complications that do not alter the surgical course or result in permanent deficits, as this difference will be apparent from the classification.

4.2 | Limitations and future perspective

Several important adverse effects of the presurgical and postoperative course of epilepsy surgery are not addressed in the protocol. Apart from the surgical, medical, and neurological complications reported here, serious adverse events during seizure monitoring (such as injuries and status epilepticus), significant postoperative neuropsychological impairments, and serious psychiatric adverse effects, need to be recorded and followed by each center. Patient-reported outcomes and quality of life are other important aspects to be included in complementary studies.

Cognitive changes are common after epilepsy surgery, depending on the side and type of surgery as well as on patient age and cognitive function at baseline. The most consistently reported cognitive impairment is decline in

verbal memory after left (dominant) temporal lobe resection in up to 40% of adult patients, which would hence be regarded as an expected adverse effect rather than a complication.^{51,52} However, a small number of patients may have an unexpectedly severe impairment in cognitive function, which would then be considered as abnormal, that is, as a complication. One way to define the cutoff for a cognitive complication could be a loss of two standard deviations or more in executive function, verbal memory, or visuospatial memory, which would appear in 3% of the patients defined by patient-based norms.⁵¹ However, it would also be necessary to consider the patient's baseline performance and decide how to account for the variety of cognitive tests used in the presurgical setting. We therefore judged that adding cognitive complications to the suggested classification would be too complex. How to define, document, and report cognitive complications needs to be further and separately discussed.

We acknowledge that apart from the items included in the present protocol, other factors may influence the risk for complications, for instance, variations in the experience of the surgical team and the medical resource availability. In addition to varying protocols for prophylaxis of venous thrombosis and infection, some surgeons advocate the use of steroids in invasive electrode procedures. Prophylactic steroids were not used in any of the centers participating in the feasibility study, and this issue may be addressed in future versions of the protocol.

Regarding the feasibility study, three of the participating centers used the classification in several different epilepsy surgery procedures, but there were only 35 complications registered, and invasive investigations were with one exception limited to SEEG implantations. Therefore, the usefulness of the protocol must be demonstrated with more participating centers and a wider range of procedures.

During the feasibility study, we found that information on the number of electrode contacts was not easily available for SEEG implantations. We included this item in the protocol for invasive diagnostic procedures based on previous studies. However, although an association between the number of electrode contacts and infectious complications has been reported for subdural electrodes,¹⁹ this has not been suggested for SEEG and depth electrode implantations. We also find this intuitively less likely, as the number of electrode contacts in grids and strips is a marker for the size of the implanted electrode, whereas this is not the case for SEEG or depth electrodes. Therefore, it seems reasonable to exclude this item for SEEG and depth implantations.

We also found some inconsistencies in the reporting of mRS for the patients who had complications. Many of the patients in this cohort were children with comorbidities.

The mRS is not designed for pediatric patients,⁵³ and it is not easily interpreted in instances of significant premorbid disability.⁵⁴ A standardized outcome measure for epilepsy surgery should take into account both normal development and any neurological deficits, which may or may not be present before surgery. Moreover, drug-resistant epilepsy often imposes difficulties in daily life, which are difficult to distinguish from the effects of impaired neurological function. If the entire clinical picture is considered, no patients will have an mRS of zero unless they are seizure-free after surgery, as this outcome would require that there are “no symptoms.” Future work is needed to develop a standardized outcome measure for daily function, which can be assessed in a simple and reliable way in epilepsy surgery patients.

The protocol will be revised continuously based on information gained from its use in everyday practice. In future revisions, formal consensus methodology can be used to improve the acceptance of the protocol.

As this protocol aims to improve the reporting of complications, it must be stressed that possible adverse events are always discussed in relation to the chances of seizure freedom or seizure reduction, which is a major determinant of patient satisfaction.⁵⁵ The proposal should therefore be regarded as a part of a comprehensive follow-up of all outcomes—positive and negative—which influence the trade-off before surgery.

5 | CONCLUSIONS

Complications in invasive diagnostic procedures and epilepsy surgery must be reported prospectively in a reproducible and standardized fashion to allow comparisons between different procedures, between different centers, and over time. To identify risk factors for complications, large-scale multicenter studies are needed. In this article, we propose a protocol that provides an evidence-based collection of items relevant for prospective reporting of complications. The protocol has been discussed within the EU-funded E-epilepsy consortium, the ILAE Commission on Surgical Therapies, and the ILAE Task Force on Pediatric Epilepsy Surgery 2013–2017. Although the protocol described here was discussed within two ILAE Commissions, it does not necessarily represent the position or policy of the ILAE. The protocol can be used as a part of the quality control of individual centers and in future studies in order to improve safety in epilepsy surgery. Separate studies are needed to improve the reporting of outcomes as regards neuropsychological function, dependency, activities of daily living, and quality of life.

ACKNOWLEDGMENTS

The study was financed by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (grants ALFGBG-517901 and ALFGBG-723151). J. Helen Cross is supported by the National Institute of Health Research (NIHR) Biomedical Research Centre at Great Ormond Street Hospital. The authors thank the E-epilepsy consortium (later incorporated into the ERN EpiCARE), the ILAE Commission on Surgical Therapies, and the ILAE Task Force on Pediatric Epilepsy Surgery, for valuable input during the preparation of the protocol. We thank Christoph Helmstaedter for helpful discussion regarding cognitive adverse effects and Martin Tisdall for his help with the feasibility study.

CONFLICT OF INTEREST

J. Helen Cross is Clinical Advisor to the national Children's Epilepsy Surgery Service in England. The remaining authors declare no conflicts of interest of relevance for this paper. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Johan Bjellvi  <https://orcid.org/0000-0001-5275-5489>

J. Helen Cross  <https://orcid.org/0000-0001-7345-4829>

Sylvain Rheims  <https://orcid.org/0000-0002-4663-8515>

Philippe Ryvlin  <https://orcid.org/0000-0001-7775-6576>

Michael R. Sperling  <https://orcid.org/0000-0003-0708-6006>

Bertil Rydenhag  <https://orcid.org/0000-0001-8472-5313>

Kristina Malmgren  <https://orcid.org/0000-0001-8485-7375>

REFERENCES

1. Arya R, Mangano FT, Horn PS, Holland KD, Rose DF, Glauser TA. Adverse events related to extraoperative invasive EEG monitoring with subdural grid electrodes: a systematic review and meta-analysis. *Epilepsia*. 2013;54:828–39.
2. Georgiadis I, Kapsalaki EZ, Fountas KN. Temporal lobe resective surgery for medically intractable epilepsy: a review of complications and side effects. *Epilepsy Res Treat*. 2013;2013:752195.
3. Hader WJ, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, Wiebe S, Kwon C-S, et al. Complications of epilepsy surgery: a systematic review of focal surgical resections and invasive EEG monitoring. *Epilepsia*. 2013;54:840–7.
4. West S, Nolan SJ, Cotton J, Gandhi S, Weston J, Sudan A, et al. Surgery for epilepsy. *Cochrane Database Syst Rev*. 2015;7:CD010541.
5. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250:187–96.

6. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. *Surgery*. 1992;111:518–26.
7. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–13.
8. Landriel Ibañez FA, Hem S, Ajler P, Vecchi E, Ciralo C, Baccanelli M, et al. A new classification of complications in neurosurgery. *World Neurosurg*. 2011;75:709–15; discussion 604–711.
9. Houkin K, Baba T, Minamida Y, Nonaka T, Koyanagi I, Iiboshi S. Quantitative analysis of adverse events in neurosurgery. *Neurosurgery*. 2009;65:587–94; discussion 594.
10. Gozal YM, Akture E, Ravindra VM, Scoville JP, Jensen RL, Couldwell WT, et al. Defining a new neurosurgical complication classification: lessons learned from a monthly Morbidity and Mortality conference. *J Neurosurg*. 2019;132:272–6.
11. Behrens E, Schramm J, Zentner J, König R. Surgical and neurological complications in a series of 708 epilepsy surgery procedures. *Neurosurgery*. 1997;41:1–9; discussion 9–10.
12. Rydenhag B, Silander HC. Complications of epilepsy surgery after 654 procedures in Sweden, September 1990–1995: a multicenter study based on the Swedish National Epilepsy Surgery Register. *Neurosurgery*. 2001;49:51–6; discussion 56–7. <https://pubmed.ncbi.nlm.nih.gov/11440459/>
13. d'Orto P, Rizzi M, Mariani V, Pelliccia V, Lo Russo G, Cardinale F, et al. Surgery in patients with childhood-onset epilepsy: analysis of complications and predictive risk factors for a severely complicated course. *J Neurol Neurosurg Psychiatry*. 2019;90:84–9.
14. Hamer HM, Morris HH, Mascha EJ, Karafa MT, Bingaman WE, Bej MD, et al. Complications of invasive video-EEG monitoring with subdural grid electrodes. *Neurology*. 2002;58:97–103.
15. Wellmer J, von der Groeben F, Klarmann U, Weber C, Elger CE, Urbach H, et al. Risks and benefits of invasive epilepsy surgery workup with implanted subdural and depth electrodes. *Epilepsia*. 2012;53:1322–32.
16. Blauwblomme T, Ternier J, Romero C, Pier KST, D'Argenzio L, Pressler R, et al. Adverse events occurring during invasive electroencephalogram recordings in children. *Oper Neurosurg*. 2011;69:ons169–75; discussion ons175.
17. Schmeiser B, Wagner K, Schulze-Bonhage A, Mader I, Wendling A-S, Steinhoff BJ, et al. Surgical treatment of mesiotemporal lobe epilepsy: which approach is favorable? *Neurosurgery*. 2017;81:992–1004.
18. De Almeida AN, Olivier A, Quesney F, Dubeau F, Savard G, Andermann F. Efficacy of and morbidity associated with stereoelectroencephalography using computerized tomography-or magnetic resonance imaging-guided electrode implantation. *J Neurosurg*. 2006;104:483–7.
19. Yang PF, Zhang HJ, Pei JS, Tian J, Lin Q, Mei Z, et al. Intracranial electroencephalography with subdural and/or depth electrodes in children with epilepsy: techniques, complications, and outcomes. *Epilepsy Res*. 2014;108:1662–70.
20. Bjellvi J, Flink R, Rydenhag B, Malmgren K. Complications of epilepsy surgery in Sweden 1996–2010: a prospective, population-based study. *J Neurosurg*. 2015;122:519–25.
21. Grivas A, Schramm J, Kral T, von Lehe M, Helmstaedter C, Elger CE, et al. Surgical treatment for refractory temporal lobe epilepsy in the elderly: seizure outcome and neuropsychological sequels compared with a younger cohort. *Epilepsia*. 2006;47:1364–72.
22. Srikiyvilaiikul T, Lerdlum S, Tepmongkol S, Shuangshoti S, Lochareernkul C. Outcome of temporal lobectomy for hippocampal sclerosis in older patients. *Seizure*. 2011;20:276–9.
23. Hedegard E, Bjellvi J, Edelvik A, Rydenhag B, Flink R, Malmgren K. Complications to invasive epilepsy surgery workup with subdural and depth electrodes: a prospective population-based observational study. *J Neurol Neurosurg Psychiatry*. 2014;85:716–20.
24. Tebo CC, Evins AI, Christos PJ, Kwon J, Schwartz TH. Evolution of cranial epilepsy surgery complication rates: a 32-year systematic review and meta-analysis. *J Neurosurg*. 2014;120:1415–27.
25. Kobulashvili T, Hofler J, Dobesberger J, Ernst F, Ryvlin P, Cross JH, et al. Current practices in long-term video-EEG monitoring services: a survey among partners of the E-PILEPSY pilot network of reference for refractory epilepsy and epilepsy surgery. *Seizure*. 2016;38:38–45.
26. Pressler RM, Seri S, Kane N, Martland T, Goyal S, Iyer A, et al. Consensus-based guidelines for Video EEG monitoring in the pre-surgical evaluation of children with epilepsy in the UK. *Seizure*. 2017;50:6–11.
27. Boon P, De Cock E, Mertens A, Trinka E. Neurostimulation for drug-resistant epilepsy: a systematic review of clinical evidence for efficacy, safety, contraindications and predictors for response. *Curr Opin Neurol*. 2018;31:198–210.
28. Revesz D, Rydenhag B, Ben-Menachem E. Complications and safety of vagus nerve stimulation: 25 years of experience at a single center. *J Neurosurg Pediatr*. 2016;18:97–104.
29. Vale FL, Pollock G, Dionisio J, Benbadis SR, Tatum WO. Outcome and complications of chronically implanted subdural electrodes for the treatment of medically resistant epilepsy. *Clin Neurol Neurosurg*. 2013;115:985–90.
30. Wiggins GC, Elisevich K, Smith BJ. Morbidity and infection in combined subdural grid and strip electrode investigation for intractable epilepsy. *Epilepsy Res*. 1999;37:73–80.
31. Wong CH, Birkett J, Byth K, Dexter M, Somerville E, Gill D, et al. Risk factors for complications during intracranial electrode recording in presurgical evaluation of drug resistant partial epilepsy. *Acta Neurochir*. 2009;151:37–50.
32. Shibata S, Kunieda T, Inano R, Sawada M, Yamao Y, Kikuchi T, et al. Risk factors for infective complications with long-term subdural electrode implantation in patients with medically intractable partial epilepsy. *World Neurosurg*. 2015;84:320–6.
33. Simon SL, Telfeian A, Duhaime AC. Complications of invasive monitoring used in intractable pediatric epilepsy. *Pediatr Neurosurg*. 2003;38:47–52.
34. Wyler AR, Walker G, Simes G. The morbidity of long-term seizure monitoring using subdural strip electrodes. *J Neurosurg*. 1991;74:734–7.
35. Rinaldo L, Brown DA, Bhargava AG, Rusheen AE, Naylor RM, Gilder HE, et al. Venous thromboembolic events in patients undergoing craniotomy for tumor resection: incidence, predictors, and review of literature. *J Neurosurg*. 2019;132:10–21.
36. Beimer NJ, Buchtel HA, Glynn SM. One center's experience with complications during the Wada test. *Epilepsia*. 2015;56:e110–3.
37. Haag A, Knake S, Hamer HM, Boesebeck F, Freitag H, Schulz R, et al. The Wada test in Austrian, Dutch, German, and Swiss

- epilepsy centers from 2000 to 2005: a review of 1421 procedures. *Epilepsy Behav.* 2008;13:83–9.
38. Loddenkemper T, Morris HH, Moddel G. Complications during the Wada test. *Epilepsy Behav.* 2008;13:551–3. <https://pubmed.ncbi.nlm.nih.gov/18590981/>
 39. Rocha-Filho PA. Post-craniotomy headache: a clinical view with a focus on the persistent form. *Headache.* 2015;55:733–8.
 40. Patel N, Rao VA, Heilman-Espinoza ER, Lai R, Quesada RA, Flint AC. Simple and reliable determination of the modified rankin scale score in neurosurgical and neurological patients: the mRS-9Q. *Neurosurgery.* 2012;71:971–5; discussion 975.
 41. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke.* 1988;19:604–7.
 42. Dorfer C, Widjaja E, Ochi A, Carter Snead Iii O, Rutka JT. Epilepsy surgery: recent advances in brain mapping, neuroimaging and surgical procedures. *J Neurosurg Sci.* 2015;59:141–55.
 43. Allibone JB, Harkness WJ, Hayward RD. Craniotomy-related complications in a paediatric neurosurgery unit—a prospective study. *Br J Neurosurg.* 1999;13:148–53.
 44. Cardinale F, Rizzi M, Vignati E, Cossu M, Castana L, d'Orio P, et al. Stereoelectroencephalography: retrospective analysis of 742 procedures in a single centre. *Brain.* 2019;142:2688–704.
 45. McGovern RA, Ruggieri P, Bulacio J, Najm I, Bingaman WE, Gonzalez-Martinez JA. Risk analysis of hemorrhage in stereo-electroencephalography procedures. *Epilepsia.* 2019;60:571–80.
 46. Schmidt RF, Wu C, Lang MJ, Soni P, Williams KA, Boorman DW, et al. Complications of subdural and depth electrodes in 269 patients undergoing 317 procedures for invasive monitoring in epilepsy. *Epilepsia.* 2016;57:1697–708.
 47. Basheer SN, Connolly MB, Lautzenhiser A, Sherman EM, Hendson G, Steinbok P. Hemispheric surgery in children with refractory epilepsy: seizure outcome, complications, and adaptive function. *Epilepsia.* 2007;48:133–40.
 48. Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain.* 2003;126:556–66.
 49. Winston GP. Epilepsy surgery, vision, and driving: what has surgery taught us and could modern imaging reduce the risk of visual deficits? *Epilepsia.* 2013;54:1877–88.
 50. Winston GP, Daga P, White MJ, Micallef C, Miserocchi A, Mancini L, et al. Preventing visual field deficits from neurosurgery. *Neurology.* 2014;83:604–11.
 51. Helmstaedter C. Cognitive outcomes of different surgical approaches in temporal lobe epilepsy. *Epileptic Disord.* 2013;15:221–39.
 52. Sherman EM, Wiebe S, Fay-McClymont TB, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, et al. Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates. *Epilepsia.* 2011;52:857–69.
 53. Engelmann KA, Jordan LC. Outcome measures used in pediatric stroke studies: a systematic review. *Arch Neurol.* 2012;69:23–7.
 54. Bruno A, Switzer JA, Durkalski VL, Nichols FT. Is a prestroke modified Rankin Scale sensible? *Int J Stroke.* 2011;6:414–5.
 55. Seiam AH, Dhaliwal H, Wiebe S. Determinants of quality of life after epilepsy surgery: systematic review and evidence summary. *Epilepsy Behav.* 2011;21:441–5.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Bjellvi J, Cross JH, Gogou M, Leclercq M, Rheims S, Ryvlin P, et al. Classification of complications of epilepsy surgery and invasive diagnostic procedures: A proposed protocol and feasibility study. *Epilepsia.* 2021;62:2685–2696. <https://doi.org/10.1111/epi.17040>