

ILAE Commission Report

Proposal for a New Classification of Outcome with Respect to Epileptic Seizures Following Epilepsy Surgery

Commission on Neurosurgery of the International League Against Epilepsy (ILAE) 1997–2001:

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EDITOR'S NOTE

The Executive Committee of the ILAE has approved the following report of the Commission on Neurosurgery for publication as a *PROPOSAL*. The Commission seeks input regarding the document and welcomes any suggestions for changes, including additions, modifications, and deletions. The proposal, therefore, is very much a draft document, which will likely require further alteration before being accepted as a new outcome classification for use with epilepsy surgery.

Feedback may be in the form of either Letters to the Editor or directly to Professor H. Gregor Wieser, Chairman of the Commission on Neurosurgery.

Timothy A. Pedley, M.D.
Editor-in-Chief, *Epilepsia*

During the Ninth International Symposium on "Epilepsy Surgery" held in Cleveland from June 22–26, 1998 (Organizers, Hans O. Lüders and Youssef Comair), there were satellite workshops on "Classification of Outcome with respect to Epileptic Seizures" and "Classification of Outcome with respect to Quality of Life." The participants of the Workshop on Seizure Outcome, W. T. Blume, D. Fish, E. S. Goldensohn, A. Hufnagel, D. King, H. Lüders, M. R. Sperling, and H. G. Wieser (Chairman), developed the following proposal for a new classification (see Table 1). This proposal was then discussed

by the Commission on Neurosurgery of the International League Against Epilepsy (ILAE) and accepted unanimously by the members of this Commission [Minutes, ILAE Commission on Neurosurgery Meeting Orlando, December 7, 1999: Members present: Paul Boon, Helen Cross, Walter van Emde Boas, John Gates, Hans Holthausen, Andreas Hufnagel, Yoshiaki Mayanagi, Cigdem Oezkara, Charles Polkey, Jean Regis, Bertil Rydenhag, Susan Spencer, Heinz Gregor Wieser]. Useful comments from Prof. Jerome Engel, Jr., also were incorporated into the final document.

We propose using this new classification to report the patient's outcome class and frequency of postoperative seizure days on an annual basis at each anniversary date after the surgery (i.e., the first year starts at the date of surgery). The classification of a patient may change over successive years. Classes 1–3 refer to absolute postoperative seizure events (i.e., seizure days). Classes 4–6 refer to relative changes with respect to the preoperative seizure constellation (in the case of a marked improvement, class 4; no significant postoperative changes, class 5; and postoperative worsening, class 6). *Baseline* is always a defined period before surgery.

Data should be reported in such a way that *patients who have been seizure-free since surgery* are readily identified. Moreover, class 1 allows a distinction to be drawn between patients who are completely seizure free and have no auras without antiepileptic drugs (AEDs) and those who are completely seizure free and have no auras but still take AEDs.

The participants of the Cleveland Workshop and authors of the initial proposal discussed in detail the pos-

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TABLE 1. Proposal for a new classification of outcome with respect to epileptic seizures

Outcome classification	Definition
1	Completely seizure free; no auras
2	Only auras; no other seizures
3	One to three seizure days per year; ± auras
4	Four seizure days per year to 50% reduction of baseline seizure days; ± auras
5	Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; ± auras
6	More than 100% increase of baseline seizure days; ± auras

sibility of developing a “combined” seizure outcome and quality-of-life classification. However, we concluded that now it would be best to formulate two separate classification systems, each of which should be applied in parallel to the same population. The two outcome measures should be such that they can be merged easily. Dr. Dodrill’s workshop on “Classification of Outcome with Respect to Quality of Life” will be working on the complementary classification system.

We agreed that studies of outcome should try to use multiple yearly outcome data points and strive for uniform end points in their analyses.

Two lines of reasoning led us to propose a modification of Engel’s widely used classification (see Table 2):

1. Disadvantages of the current Engel’s classification system

- Although Engel’s classification (1) is now used extensively, results from different centers cannot be compared easily. Engel’s category “worthwhile improvement” is ambiguous and is therefore calculated or interpreted differently from center to center. Some centers, for example, ask for a ≥90% reduction; others accept ≥50% or ≥60% or ≥75% seizure reduction. Baselines are often not clearly defined. In addition the term “worthwhile” requires a subjective judgment that may not be entirely justified, so this term is best avoided.
- To facilitate comparison with AED drug trials, which commonly use “≥50% seizure reduction” as an end point, we propose including a surgical seizure outcome category “≥50% seizure reduction.”
- In Engel’s category I, seizure-free patients are included with others who still have seizures. Although Engel’s category IA refers to absolutely seizure-free patients, in reality, most centers do not report outcomes using Engel’s subcategories. Therefore, the actual number of seizure-free patients is frequently obscure. For obvious reasons, the seizure-free patient group is the most impor-

tant, for both clinical and scientific purposes. Because auras are simple partial seizures, a mixture of pure seizure-free patients with those having still auras should be avoided.

- A category of postsurgical “worsening” of seizures is needed.
2. Principles underlying a new classification system
- The classification system should be as simple as possible. The previous experience of various groups dealing with outcome measures (e.g., ILAE Commissions on Epilepsy Surgery and Outcome Classification) shows clearly that only a simple proposal has a realistic chance for worldwide application. A new proposal therefore should avoid difficult-to-define terms, such as “worthwhile” and “disabling.”
 - The classification system should be equally applicable to an individual person and to a sample population, both on a year-by-year basis, and (most important) cumulatively to the “last available outcome.” It should be applicable independently to different seizure types to meet the needs of “palliative” procedures, such as corpus callosum section, in which very often only one seizure type is targeted.
 - It should reasonably handle the special difficulties related to status epilepticus and the differentiation between nocturnal and diurnal seizures. Counting “seizure days” instead of the absolute number of seizures is a more realistic measure. In this context, a “seizure day” is defined as a 24-h period.

TABLE 2. Engel’s Classification of Postoperative Outcome (1)

Class I: Free of disabling seizures ^a
A: Completely seizure free since surgery
B: Nondisabling simple partial seizures only since surgery
C: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years
D: Generalized convulsions with AED discontinuation only
Class II: Rare disabling seizures (“almost seizure free”)
A: Initially free of disabling seizures but has rare seizures now
B: Rare disabling seizures since surgery
C: More than rare disabling seizures since surgery, but rare seizures for the last 2 years
D: Nocturnal seizures only
Class III: Worthwhile improvement ^b
A: Worthwhile seizure reduction
B: Prolonged seizure-free intervals amounting to greater than half the followed-up period, but not <2 years
Class IV: No worthwhile improvement
A: Significant seizure reduction
B: No appreciable change
C: Seizures worse

^a Excludes early postoperative seizures (first few weeks).

^b Determination of “worthwhile improvement” will require quantitative analysis of additional data such as percentage seizure reduction, cognitive function, and quality of life.

- The classification should account for the fact that some patients rarely have seizures that occur in clusters, or even an episode of status epilepticus, in response to, or associated with, highly provocative situations, such as antiepileptic drug (AED) discontinuation. Taking these circumstances into consideration, tabulating “seizure days” rather than an absolute number of seizures is preferable and more meaningful clinically.
 - Finally the classification should be such that further refinements can be adopted easily. Examples are the categories “last available outcome” and “completely seizure free since surgery,” or the “running-down phenomenon” of auras. The study of the latter phenomenon will certainly be facilitated using the proposed classification system.
3. The following points were discussed in depth, but not included
- We consider it desirable to know if patients are seizure free after surgery with or without AEDs. However, we concluded that two separate categories are unjustified, because many patients who become seizure free after surgery continue to take AEDs to avoid risking a possible recurrence that might be associated with discontinuation of AEDs. Because it is impossible to determine how many patients would be seizure free without AEDs, we decided against splitting category 1 into “seizure free without AEDs” and “seizure free with AEDs.”
 - As already mentioned, we considered “quality of life” outcome measurement to be very important. Currently it is either not reported or not comprehensive. The inclusion of the term “worthwhile” in the seizure outcome classification may be clinically useful, but it might also prevent a more comprehensive quality-of-life assessment. We agreed, therefore, to avoid a quality-of-life measure in a seizure outcome classification and to use a separate quality-of-life outcome scale in parallel. Quality-of-life outcome measurement should be comprehensive and reflect behavioral, schooling, occupation, psychosocial, self-sufficiency, marriage and reproduction, and mental and cognitive domains.
 - Some authors (2,3) have argued that an outcome classification should allow investigators to measure whether surgery reached the contracted aim (individually formulated in precise terms). Although we found this interesting, we concluded that it would not be possible to integrate such a measure into a widely usable classification system.

- We discussed the fact that there is a growing need to measure postsurgical results in a way that allows “cost–benefit” analysis. We found that this might be better covered in a quality-of-life classification. Nevertheless, the proposed seizure outcome classification, when properly used on a year-by-year basis, should provide cumulative outcome data that will permit other, more sophisticated analyses, beyond those described here.

Comments to Table 1

1. Seizure outcome class is determined for each year at annual intervals after the date of surgery. Patients may change from one classification to another from year to year.
2. Seizures during the first month after surgery are not counted. These may be related to the surgery itself (“neighborhood seizures”) and do not predict long-term outcome.
3. An aura is a simple partial seizure that is not observable by witnesses (i.e., a purely subjective experience that does not affect the patient’s function). Auras should be counted only if they are of short duration and are similar or identical to the auras the patient experienced before surgery. If the history is unclear, auras should not be counted. Postoperatively, many patients are anxious and may report subjective feelings that are not epileptic.
4. Class 3 is included because it is quite common for patients to have “rare seizures” postoperatively. These are often nocturnal and often tonic–clonic. It is practical experience that some patients have such seizures only on certain (usually provocative) occasions, and as a result, usually can cope fairly well.

For statistical reasons, classes 4, 5, and 6 can be replaced by an absolute scale denoting either the percentage improvement (classes 4 and 5) or the extent of worsening (classes 5 and 6) expressed in 10% increments/decrements related to the baseline seizure frequency expressed in seizure days.

5. A “seizure day” is a 24-h period with one or more seizures. This may include an episode of status epilepticus.
6. The number of “baseline seizure days” is calculated by determining the seizure-day frequency during the 12 months before surgery, with correction for the effects of AED reduction during diagnostic evaluation. We admit that this classification works adequately only in patients with chronic epilepsy who have had seizures for >12 months. Exceptions may include patients who

TABLE 3. Reporting seizure outcome using the new classification system

Year 0 (preoperative baseline) (n = 400)	Year 1 (n = 369)	Year 2 (n = 331)	Year 3 (n = 287)	Year 4 (n = 261)	Year 10 (n = 125)
Class 1: Completely seizure free; no auras	208 (56%)	187 (56%)	155 (54%)	140 (54%)	71 (57%)
Class 1a: Completely seizure free <i>since surgery</i> ; no auras	208 (56%)	166 (50%)	121 (42%)	102 (39%)	42 (34%)
Class 2: Only auras; no other seizures	49 (13%)	38 (12%)	27 (9%)	21 (8%)	7 (6%)
Class 3: 1–3 seizure days per year; \pm auras	27 (7%)	30 (9%)	30 (11%)	25 (10%)	13 (10%)
Class 4: 4 seizure days per year to 50% reduction of baseline seizure days; \pm auras	50 (14%)	44 (13%)	43 (15%)	45 (17%)	14 (11%)
Class 5: <50% reduction of baseline seizure days to 100% increase of baseline seizure days; \pm auras	35 (10%)	32 (10%)	32 (11%)	30 (11%)	20 (16%)
Class 6: >100% increase of baseline seizure days; \pm auras	0	0	0	0	0

Recently compiled “realistic” outcome data (Zurich amygdalohippocampectomy series) are used for illustrative purposes: Data are plotted for postoperative years 1–4, and year 10. Year 10 serves also to show how the last available outcome (using the year before the last surgical anniversary) can be easily added into such an outcome classification. Note also that class 1 has been split for the purpose of reporting the number of patients who are “completely seizure free since surgery.”

have outcomes in classes 1–3. For patients who had seizures begin <12 months before surgery and who have outcomes other than 1, 2, and 3, no baseline will be available. In rare instances in which seizure onset is <12 months, and patients do not belong in outcome classes 1–3, the baseline can be approximated, but this should be properly documented. For instance, in a patient who had onset of seizures 9 months before surgery, with one seizure day in the first month, two in the second, three in the third, building up to several a week before surgery, the last month before surgery could be used as baseline, but this has to be documented.

7. In Classes 4, 5, and 6, the change of seizure-free days with reference to baseline should be further detailed at least in 10% subcategories, or (better) in absolute numbers to allow cumulative data reporting.
8. Class 5 means that the surgery neither significantly improved nor significantly worsened the patient’s clinical situation. After discussion and advice from statisticians, we decided for the 100% increase of baseline seizure days (vs. 50%). It is justified for mathematical and biologic reasons to assume that seizure frequencies and their changes after surgery have a normal logarithmic distribution. This implies that a 50% decrease is equivalent to a 100% increase.
9. In the year-by-year reporting of class 1 outcomes, we recommend including a subgroup identified as “completely seizure free *since surgery*; no auras” (see example, Table 3 and Fig. 1). We also recommend that those patients designated class 1 without AEDs be reported separately.
10. The “last available outcome” can be indicated in a separate column, provided that there be a minimal follow-up of 1 year after surgery. It should be further specified by mean \pm standard deviation,

and minimal and maximal follow-up. The last available year must be included. Example: consider that a patient had surgery on September 5, 1992, and was followed up to the end of July 1998. The period that counts for the “last available outcome” would then be September 5, 1996, to September 5, 1997. (See also legend for Table 3). Only in circumstances in which the length of follow-up is critical, the last available outcome can be calculated for the immediately previous 12-m period (i.e., in this example, July 31, 1997, to July 31, 1998). It should be indicated whether the year before the last surgical anniversary or the last 12-m period is taken into account.

General comments

Although considerable effort over the last decade has been put into developing outcome measures, the interpretation of published reports on the long-term outcome of patients undergoing epilepsy surgery has been difficult because of several methodologic problems. These include lack of appropriate, standardized classification systems for both seizure outcome and quality-of-life outcome over time (4–7).

The task of revising Engel’s currently already widely used seizure-outcome classification is justified only if it is done in as thoughtful a manner as possible, and if it is generally accepted by the international epilepsy community. We believe that this new seizure-outcome proposal is a useful improvement, assuming that centers will have the data and will take the trouble to calculate outcome on the basis of preoperative seizure days. Although for retrospective studies, many centers will be unable to do this, or will use it in addition to the current Engel classification, we believe strongly that it should be used for prospective studies, because of its discussed advantages.

With the publication of this proposal, we hope to obtain sufficient input to revise and refine this proposed

New seizure outcome classification: Year-by-year

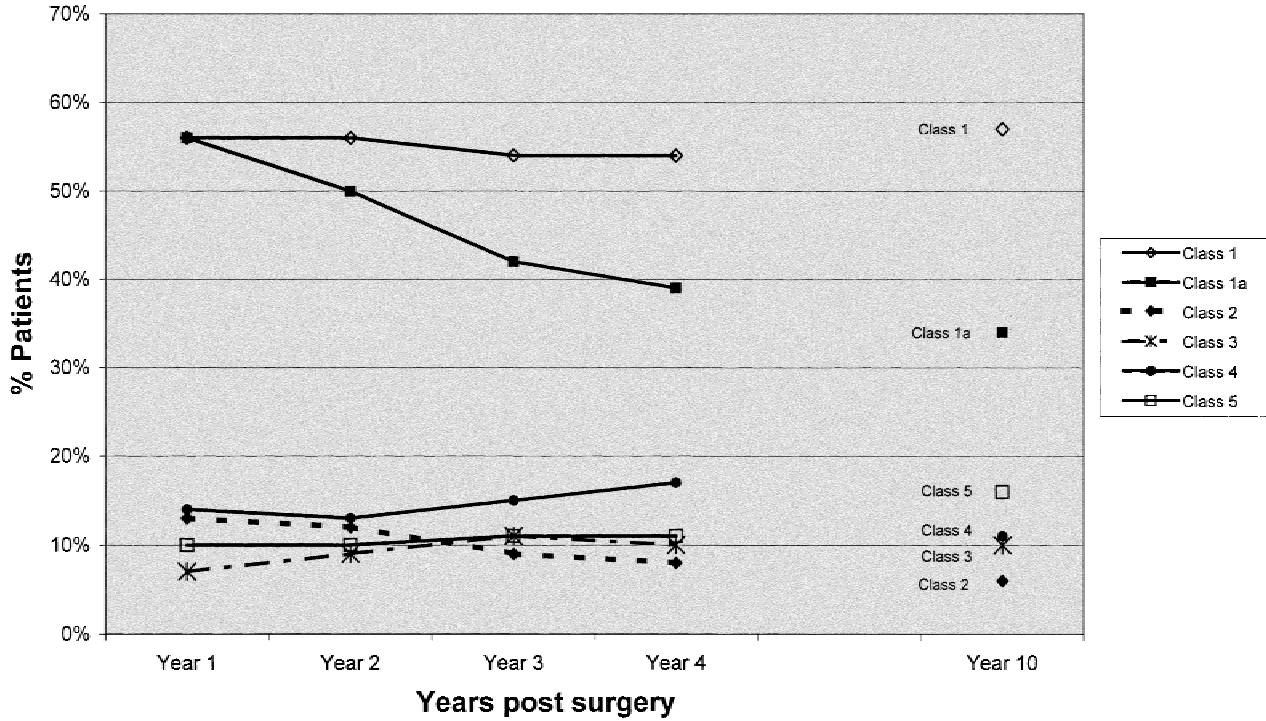


FIG. 1. Graphic display of Table 3. For reasons of clarity, class 6 is not plotted.

classification to a point where it is acceptable to the major centers doing epilepsy surgery around the world.

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