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Highlights

Epilepsy surgery carries well defined surgical and neurological risks, which need to be balanced against the risks of morbidity and mortality from continued seizures, and the chances of seizure remission with surgery.

The frequency of unexpected persistent neurological adverse events, which can affect quality of life, was 2.2% following epilepsy surgery.

Subdural EEG recordings were associated with increased risk of serious site-specific infection

Somatic complications of epilepsy surgery over 25 years at a single center

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Abstract

Introduction

Epilepsy surgery is an effective treatment for refractory focal epilepsy. Risks of surgery need to be considered when advising individuals of treatment options. We describe the frequency and nature of physical adverse events associated with epilepsy surgery in a single center.

Material and Methods

We reviewed the prospectively maintained records of adults who underwent epilepsy surgery at our center between 1990 and 2014 to identify peri/postsurgical adverse events. These were categorized into neurological deficits and those related to surgery (e.g. wound infections). Neurological deficits were categorized as expected or unexpected and into transient (≤3 months) or persistent (>3 months),

Results

There were 911 procedures with no peri-operative deaths. Persistent neurological adverse events were seen following 157 (17.2%) procedures. The most common persistent expected complication was quadrantanopia after temporal lobe resections (72/764, 9.4%). Unexpected persistent neurological complications occurred in 20 procedures (2.2%) and included: quadrantanopia (6, 0.7%); hemianopia (2, 0.2%); hemi/mono-paresis/sensory loss (9, 1%); dysphasia (10, 1%); frontalis muscle weakness (2, 0.2%); and oculomotor weakness (1, 0.1%).

106 surgery related adverse events occurred in 83 procedures, with severe infections requiring bone-flap removal in 24 (2.6%) procedures and intracranial infections in 8 (0.9%). The risk of post-resective severe infection increased by 4 fold (OR 4.32, 95% CI 2.1 to 8.9, $p<0.001$) with use of subdural EEG monitoring prior to resection. In consequence, in August 2011 we introduced antibiotic coverage in all individuals undergoing intracranial monitoring. Also, after August 2011 there was greater use of Stereo-EEG (SEEG) than subdural (OR 9.0 CI 0.36 to 224.2, $p=0.18$ ns). One complicated by severe infection. Other surgical complications included haematoma (0.3%), hydrocephalus (0.3%) and CSF leak (1.2%). None had permanent complications.

Conclusions

Adverse event rates are similar to other series. Epilepsy surgery carries well defined surgical and neurological risks. The risks of somatic adverse events, in addition to neuropsychiatric and neuropsychological complications need to be made clear to individuals considering this treatment option.

Keywords: epilepsy surgery, adverse events, neurological deficits

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1. Introduction

Surgical removal of the epileptic focus is effective for some individuals with refractory focal epilepsy, with up to 80% of those operated having seizure remissions of at least one year (Jutila et al., 2002; de Tisi et al., 2011). As in any surgical procedure, detailed knowledge of risks is a prerequisite to enable adequate pre-surgical advice to individuals. The perception of risk may be one of the major factors influencing an individual's decision to undergo surgery.

Many observational studies on epilepsy surgery outcome include adverse event data. Despite this, there are few large series specifically addressing complications. We recently published the long-term seizure outcome of epilepsy surgery at our centre (de Tisi et al., 2011) and the neuropsychological (Baxendale et al., 2012) and psychiatric complications (Cleary et al., 2012). Here we describe the frequency and nature of physical adverse events associated with epilepsy surgery in the same cohort over a 25 year period.

2. Material and Methods

We retrospectively reviewed the prospectively maintained records of adults who underwent epilepsy surgery at the National Hospital for Neurology and Neurosurgery (NHNN), between 15 February 1990, and 31 December 2014, for peri/post-surgical complications. One or more adverse events may be recorded after a single procedure.

Post-operative follow-up included: neurosurgical review at 2-3 months after surgery, neurological review at 3 and 12 months post-op, brain imaging (MRI) at 3 months after surgery and neuropsychology assessments at 3 and 12 months after surgery.

Adverse events were categorized into neurological (neurological deficits following surgery) and surgical (general adverse events related to surgery) (**Figure 1**). Neurological adverse events were categorized into transient (lasting ≤3 months) or persistent (lasting >3 months) and were further grouped into those that were expected or unexpected.

Neurological adverse events included: quadrantanopia, hemianopia, hemiparesis/sensory loss, monoparesis/ sensory loss, dysphasia, oculomotor weakness and frontalis muscle weakness.

Quadrantanopia was determined by perimetry and was recorded if it was severe enough to prevent driving in the UK. In the majority of subjects visual fields were assessed using the binocular Estermann test while in a minority Goldmann perimetry was used. For the Estermann test the following is regarded as unacceptable for driving in the UK: a central loss of a cluster of 4 or more adjoining points that is either wholly or partly within the central 20° area, a loss consisting of both a single cluster of 3 adjoining missed points up to and including 20° from fixation, and any additional separate missed points within the central 20° area and any central loss that is an extension of hemianopia or quadrantanopia of size greater than 3 missed points. Goldmann perimetry requires a field of at least 120° on the horizontal measured using a target equivalent to the white

Goldmann III4e setting and extension should be at least 50° left and right, to drive in the UK. There should be no significant defect in the binocular field that encroaches within 20° of the fixation above or below the horizontal meridian.

An expected neurological complication was defined as an anticipated sequel of a surgical procedure based on the proximity of resection to eloquent structures, for example, upper quadrantanopia following anterior temporal lobe resection, hemi/monoparesis after surgery involving the motor strip or worsened weakness following hemispherectomy. An unexpected adverse event was any neurological deficit following surgery that was not predicted to occur.

Surgery-related adverse events included: infection needing antibiotics, venous thrombosis (DVT)/ pulmonary embolism (PE), hydrocephalus, headache persisting over 3 months and affecting quality of life, and CSF leakage needing re-suturing. Infection needing antibiotics was further categorized into infection involving the surgical site or elsewhere. Surgical site infection included intracerebral and epidural abscesses, meningitis and bone flap infection necessitating removal with subsequent cranioplasty. Severe infection was defined as intracranial infection and/or bone-flap infection requiring removal.

All surgical procedures were included in the report of the total adverse event rates, demographic data, complication rates according to type of surgery, and temporal analysis of adverse events. The chi-square test was used to examine the relationship between categorical variables. A series of binary logistic regression models were used to examine likelihood of having adverse events (neurological and surgical), persistent neurological adverse events and unexpected persistent neurological adverse events between temporal and extra-temporal surgical procedures. We also performed a logistic regression model to determine the influence of age on persistent neurological complications. Odds ratios with corresponding 95% confidence intervals were calculated. P values less than 0.05 were considered significant. SPSS version 21 was used for all statistical analyses.

All individuals consented to the surgical procedures. This exercise was approved by our local Research Ethics Committee as a service evaluation that did not require individual patient consent.

3. Results

3.1 Descriptive statistics

A total of 911 procedures were performed on 887 individuals (481[55%] female). Twenty four had repeat surgical procedures. Age at surgery ranged from 16-68 years with a mean age of 34.5 SD±10.2 years. There were no surgery related deaths. The post-operative follow up period ranged between 1 year and 24 years with a median of 9 years.

Of the 911 procedures 764 (84%) were temporal; 91 (10%) frontal; 21 (2.3%) parietal; 10 (1.1%) occipital lobe resections; with 16 (1.8%) hemispherectomies; 4 (0.4%) multiple subpial transections and 5 (0.5%) corpus-callosotomies (**Table 1**).

Following 911 procedures, at least one adverse event was reported in 240 (26.3%) procedures, with a total of 157 (17.2%) neurological only (persistent/transient) and 63 (6.9%) surgical only, and 20 (2.2%) having both types. A higher percentage of extra-temporal procedures (38.8%) than temporal lobe procedures (24%) were complicated by adverse events (**Table 1**).

Out of 118 lesionectomies (temporal and extra-temporal) performed, 27 (22.9%) procedures had at least one adverse event with 16 (13.6%) procedures having only neurological adverse events (persistent/transient), 9 (7.6%) having only surgical adverse events, and 2 (1.7%) having both neurological and surgical adverse events (**Table 1).**

3.2 Neurological adverse events

Neurological adverse events were reported after 177 of the 911 procedures (19.4%) with 20 (2.2%) being unexpected persistent and 17 (1.9%) unexpected transient (**Figure 2**). Of the 764 temporal lobe resections, 135 (17.7%) had neurological adverse events with 19 (2.5%) being unexpected persistent and 9 (1.2%) unexpected transient, while 42 (28.6%) extra-temporal procedures had neurological adverse events with 1 (0.7%) having unexpected persistent and 8 (5.4%) unexpected transient neurological adverse events.

Of the total 911 procedures, persistent quadrantanopia (77, 8.5%) was the most common persistent expected adverse event and dysphasia (10, 1.1%) was the most common unexpected adverse event. Transient dysphasias (17, 1.9%) and hemiparesis/sensory-loss (7, 0.8%) were the most frequent transient expected and transient unexpected adverse events (Table 2). Seventy two of the 77 expected persistent quadrantanopias followed temporal lobe resections.

Quadrantanopia was the most common expected persistent adverse event after temporal lobe procedures (72, 9.4%) while dysphasia (10, 1.3%) was the most frequent unexpected persistent neurological adverse event. Persistent visual field defects including quadrantanopia and hemianopia were common expected adverse events after extratemporal procedures (9.5%), followed by hemi/monoparesis (6.8%)(**Table 2**).

Logistic regression analysis showed no association between persistent neurological adverse events and age at operation (OR-1.01; 95% CI 0.97, 1.05; p=0.54). Logistic regression models predicted higher odds of having adverse events (combined neurological and surgical) (OR 2.01; 95% CI 1.39, 2.91; p<0.001) and neurological adverse events (OR 1.86; 95% CI 1.25, 2.79; p<0.001) following extra-temporal procedures compared to temporal procedures. After adjustment for gender of the patient and age at surgery, there were higher odds of having adverse events (combined neurological and surgical) (OR 2.14; 95% CI 1.48, 3.10; p<0.001) in extra temporal procedures compared to temporal procedures

3.3 Surgical adverse events

There were 106 surgical adverse events following 83 of the 911 procedures. Superficial infections at the surgical site (35, 3.8%) were the most common adverse events, followed by infections requiring bone flap removal (24, 2.6%); persistent headache (16, 1.8%) and intracranial infections including meningitis (8,

0.9%)(**Table 3**). 7.6% (58/764) of temporal lobe procedures had surgical adverse events (78 total adverse events) compared with 17% (25/147) of extratemporal procedures (28 total adverse events) ($\chi 2$= 13.2, p=0.0003).

Severe infections, defined as intracranial infection and those requiring bone flap removal were more common 8.9% (15/168) in those who had undergone intracranial EEG monitoring. Severe infection with subdural electrodes (with or without depth electrodes) was 9.6% (14/148) prior to surgery compared with 2.4% (18/763) in those who had not undergone subdural monitoring. This amounted to a 4 fold increase in risk with subdural recordings (OR 4.32, 95% CI 2.1 to 8.9, p<0.001).

The total infection rate for temporal lobe procedures was 6.5% (50/764) while it was 15% (22/147) with extra temporal procedures ($\chi 2$=12.01, p=0.0005). This higher infection rate was the main contributor towards adverse events in extra-temporal procedures. Extra temporal procedures were 6.7 times more likely (CI 4.5, 9.8, p<0.0001) to have intracranial monitoring (49%, 72/147) than temporal procedures (12.5%, 96/764), which explains the higher infection rates and total adverse event rates with extra-temporal procedures.

The infection rates associated with subdural EEG monitoring led to a revision of practice in August 2011 including the introduction of prophylactic antibiotic administration (typically Teicoplanin) for the duration of the intracranial monitoring. We did not use prophylactic antibiotics prior to August 2011. The rate of severe infections with subdural grids prior to August 2011 was 9.2% (11/120). Since after that time, the severe infection rate with subdural grids was not significantly different at 10.7% (3/28). The median duration of subdural grid recordings was the same at 8 days, in both those with, and without, severe infections (p=0.53). Moreover, there was widespread usage of SEEG rather than subdural grids after August 2011. “SEEG only” approach was utilized in only 2/122 (1.6%) procedures prior to August 2011. After August 2011, 18/46 (39%) underwent SEEG only monitoring prior to surgery and only 1 (2%, 1/46) was complicated by severe infections (OR 9.0 CI 0.36 to 224.2, p=0.18 ns).

Other adverse events which were not classified under the above categories included: dental damage 1 (0.1%), ulnar neuropathy 2 (0.2%) and chemical meningitis (culture negative/aseptic meningitis attributable to neurosurgery) (2, 0.2%). Chemical meningitis was a transient adverse event while the others lasted for more than 3 months

3.4 Adverse events involving lesionectomies

There were 118 (13%) lesionectomies performed in the whole series during this period which were complicated by the following neurological adverse events: quadrantanopia (8, 6.8%), hemianopia (2, 1.7%), hemiparesis/sensory loss (1, 0.8%), monoparesis/sensory loss (2, 1.7%), dysphasia (4, 3.4%), frontalis muscle weakness (1, 0.8%). The total neurological adverse event rate for lesionectomies was 15.3% (18/118).

Surgery-related adverse events of lesionectomies included CSF-leak (1, 0.8%) superficial infection (3, 2.5%), infection requiring bone flap removal (4, 3.4%) and extra-surgical site infections (2, 1.7%).

3.5 Temporal analysis

During the last 5 years (2010-14) of this cohort, relatively more people have had extra temporal surgery (27.6% of all procedures), compared with 14.7% in the first 5 years (1990-1994). This was not associated with an increase in expected persistent neurological adverse events (**Table 4**). During the last 5 years, a higher proportion of individuals have undergone intracranial EEG monitoring (34.9%), compared with the 1990s (10%).

4. Discussion

Direct comparisons of adverse event rates with other series are difficult as different definitions of adverse events have been used, with differences in the range of procedures, in the clinical characteristics of the cohorts, and in data collection methods.

In a systematic review of 76 series with different methodologies, 5% major and 11% minor neurological adverse events were found (Hader et al., 2013). Major adverse events were defined in a similar way we used. Our cohort had a persistent unexpected neurological adverse event rate of 2.2% and transient unexpected rate of 1.9%, which were lower than the quoted rates. The review, however, also included children, who had higher adverse event rates (11.2% vs. 5.5%; including minor neurological adverse events) than adults, which may have contributed towards a rate higher than ours. The higher rate reported in the review may also have included both expected and unexpected adverse events (as no such categorization was made). Different definitions for neurological adverse events in the paediatric age group may also contribute to the difference.

A recent prospective Swedish study of 865 procedures reported a total major adverse event rate of 3% and minor adverse event rate of 7.5% (Bjellvi et al., 2015). Only unexpected post-operative neurological impairment was recorded, comparable with our unexpected neurological adverse events. The major neurological adverse event rate was 2.9% while the minor neurological adverse events rate was 3.6%, with slightly fewer adverse events seen in our cohort than in the Swedish cohort

The most severe physical adverse events of epilepsy surgery are the neurological adverse events affecting vision, motor system (especially hand function) and speech that do not resolve and therefore have the potential to affect long-term quality-of-life (Hader et al., 2013). Dissatisfaction after surgery, even in those who are seizure free is mainly related to post-operative neurological deficits (Macrodimitris et al., 2011). Permanent neurological consequences of resective surgical procedures are often associated with the site of the procedure. Our findings suggest that persistent unexpected neurological adverse events after surgery are low. The acceptance of an expected persistent neurological adverse event by an individual suggests that some are willing to accept certain neurological deficits to be seizure-free.

The review found 1.5% major and 5.1% minor surgical adverse events (Hader et al., 2013). Our cohort had a total procedure related adverse event rate of 9.1%, higher than in the review. This rate is also higher than the Swedish study (5.2%) (Bjellvi et al., 2015). Late surgical adverse events, such as hydrocephalus developing several months after surgery, would not, however, have been included in the Swedish study as adverse events

were specifically addressed only during the post-operative in-hospital stay and at follow-up 3 months after surgery. Such late adverse events were reported in our cohort, which had continuing follow-up for up to 24 years (median 9 years).

Our infection rate (7.9%) was a major contributor to the total adverse events rate, with 2.6% requiring bone-flap removal and 0.9% having intracranial infection. A higher rate of infection was associated with subdural EEG monitoring.

A higher number of intracranial electrodes and longer duration of monitoring has been associated with increased frequency of adverse events (Hedegärd et al., 2014). However, we did not find any significant difference between duration and severe infection in our cohort. In one review, infections were the most common type of adverse events in invasive EEG monitoring with a prevalence of 5.3% (2.3% neurological infections and 3.0% superficial infections) (Arya et al., 2013). Some series reported infection rates as high as 15% (Blauwblomme et al., 2011; Simon et al., 2003). In one prospective study, the infection rate was higher if more than 100 electrode contacts (combined subdural grid and strip electrodes) were used, if more than 10 electrode cables were present, or if electrodes remained implanted for more than 14 days (Wiggins et al., 1999). Widespread usage of SEEG rather than subdural grids occurred after August 2011 in our cohort and only one was complicated by severe infection.

Several series have indicated age as a risk factor for adverse events in epilepsy surgery (Grivas et al., 2006; Rydenhag and Silander, 2001). In some studies, however, there was no difference in adverse events rates for individuals younger or older than 50 years (Patra et al., 2014; Murphy et al., 2014). The Swedish study showed a positive association with age and adverse events rate (Bjellvi et al., 2015). We found no association between age and occurrence of persistent unexpected neurological adverse events.

We carried out a sub-analysis of somatic adverse events of both temporal and extra-temporal resections. The following discussion focuses mainly on adverse events of temporal lobe resections to facilitate comparison with similar large series. Our neurological adverse event rate was comparable to rates reported in temporal lobe resections series. A review (Georgiadis et al. 2013) quoted the occurrence of hemiparesis post-operatively in adults of up to 5%, with a wide range of severity, duration, and rehabilitation rates. Dysphasia occurred in 1.7 - 7.7%, and this was permanent in 0.9%. Trochlear nerve palsy has been reported to occur in 2.6% - 19% following temporal lobe resections. In the vast majority of cases, post-operative diplopia spontaneously resolved with no sequelae. In contrast, post-operative visual field defects were permanent. Their incidence rates ranged from 1.8%-69%. In the vast majority of the reported series, these visual field defects were superior quadrantanopias. Hemianopia was reported in 1.8%-5.8%. Palsy of the frontal branch of the facial nerve was seen between 1.7% and 2.6% of temporal lobe procedures.

Post-operative infection rates of 1%-4.7% have been reported after temporal lobe resection (Georgiadis et al. 2013). The incidence of meningitis was 1.8%-4.7%. The infection rate in our series of temporal lobe resection was 6.5%. The incidence of post-operative haematoma was 1.8% - 3.8% and DVT occurred in 1.8% of individuals (Georgiadis et al. 2013). Our rates were lower than these.

A recent meta-analysis (Tebo at al., 2014) of post-surgical adverse events between 1980 and 2012 suggested that the most frequent complications after temporal lobectomy were neurological complications (19.3%), which were persistent in 3.8%. The total neurological complication rate in our temporal lobe series (17.7%) was lower, although persistent adverse events were much higher (16.4%). This may have been due to differences in definitions whereby cerebral vascular events (which can cause persistent neurological deficit) were defined as separate from neurological deficits in the review.

Superior quadrantanopia in temporal lobe resections is the commonest adverse event and was seen in 10.5% of temporal lobe procedures in our cohort. This adverse event results from injury to Meyer's loop as it passes through the roof of the lateral ventricle (Vale et al., 2013). Minor, non-clinically significant injury to Meyer's loop may occur during surgery, resulting in a field deficit only detectable by visual field perimetry, and not by the individual or by a confrontational visual field examination (Grivas et al., 2006). Different visual field examination methodologies may provide different detection rates (Manji and Plant, 2000; Nilsson et al., 2004). An incidence of field deficit of 47% when using the Esterman method, and 54% with Goldman perimeter has been reported (Chen et al., 2009).

The use of preoperative diffusion imaging and tractography can help in outlining the optic radiation (Powell et al., 2005). Registration of the tractography data on the preoperative neuro-navigational planning may mitigate the risk to the optic radiation, without compromising seizure outcome (Winston et al., 2014).

Post-operative hemiparesis after temporal lobe resection are due to vasospasm or cerebral oedema secondary to surgical manipulation (Heller et al. 2009; Schaller 20045), with persistent hemiparesis usually due to damage to vessels supplying the internal capsule (Shorvon and Moran, 2009). We found persistent hemi/monoparesis after 0.8% of temporal lobe resections.

Permanent dysphasia may occur when a dominant anterior temporal lobe resection is extended too far posteriorly or when a lesionectomy is carried out in or under the posterior temporal neocortex (Roberti et al., 2007). The anatomical location of language function in individuals with temporal lobe epilepsy can be extremely variable, and dysphasia may occur even if the resection avoids the conventional anatomical locations of eloquent language cortex. The risk can be reduced but not eliminated by preoperative language mapping. Unexpected persistent dysphasia was seen in 1.3% of temporal lobe procedures in our cohort.

The frontal branch of the facial nerve superior to the zygoma courses within the superficial temporal fascia. This is therefore vulnerable during skin incision, especially in temporal lobe resections. This was damaged following 3.5% of temporal lobe resections. Surgical adverse events related to the skin incision or the craniotomy may be prevented by employing interfascial dissection to avoid injuries to the frontal branch of the facial nerve and thus accomplish a better post-operative cosmetic result (Georgiadis et al. 2013; Roberti et al., 2007).

The meta-analysis (Tebo at al., 2014) found higher rates of neurological deficit in extra-temporal resections and also higher rates of infection/ meningitis compared to temporal resections (temporal vs extra temporal neurological deficits- 19.3% vs 23.8%, infection 1.4% vs 3.1%). This was similar to our findings. The

additional risk of intracranial electrode implantation may explain this difference as this was more likely with extra-temporal resections.

Persistent headache was seen after 1.8% of total procedures in our cohort. Currently, in the International Classification of Headache Disorders for a headache to be classified as "headache attributed to craniotomy," the craniotomy needs to have been performed for reasons other than for traumatic brain injury, and the headache needs to have started within 7 days after the surgery. If the pain lasts for less than 3 months, the headache is classified as acute; if not, as persistent (Rocha-Filho et al., 2015).

The majority of individuals report headaches on the same side as, and at the site of, the surgery. The most frequent pattern is a "tension-type headache" pattern. Allodynia at the site of the surgical scar is reported by 82% and is considered to be a problem by 19%. "Tenderness" at the incision site can last for an average of 12 months (Mosek et al., 1999).

Retrospective studies have shown a range in the incidence of headache from 0% to 100 % (Rocha-Filho et al., 2015). One study investigated 145 people who underwent anterior temporal lobe resections for intractable epilepsy over a 9-year period (Kaur et al., 2000). To eliminate confounding causes of headache, all individuals studied were seizure-free, none had progressive mass lesions or persisting vascular anomalies, and none had major complications of surgery. Six per cent complained of headaches that lasted for more than 2 months but less than 1 year, and 12% had on going headaches 1 year post-operatively. Of these, a quarter had medically uncontrolled headaches, whilst a third continued to require regular analgesia a year after surgery.

Possible causes of post-craniotomy headache include meningeal inflammation (Jackson et al. 2000), nerve compression, nerve entrapment, muscular and meningeal fibrosis (Harner et al., 1995) neuromas or nerve entrapment in a scar (Ferreira et al., 2012). Most individuals with chronic pain can be successfully treated with a combination of pharmacological and non-pharmacological approaches (de Gray and Matta, 2005).

5. Conclusion

Epilepsy surgery carries well defined surgical and neurological risks. The risks of somatic adverse events, in addition to neuropsychiatric and neuropsychological complications, need to be made clear to individuals considering this treatment option, and balanced against the risks of morbidity and mortality from continued seizures, and the chances of seizure remission with surgery. There is scope to reduce the risks of complications and this requires on-going sustained efforts.

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Disclosure of Conflicts of Interest

None of the authors have any conflict of interest to disclose in relation to this work.

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Table 1: Descriptive analysis of procedures with adverse events

	Total (no,%)	Number (%) of procedures with adverse events			
		Total	*Neurological alone	Surgical alone	*Neurological+ surgical(combined)
Operation type (anatomical)					
Temporal lobe	764 (100)	183 (24.0)	125 (16.4)	48 (6.3)	10 (1.3)
Extratemporal	147 (100)	57 (38.8)	32 (21.8)	15 (10.2)	10 (6.8)
Frontal	91 (100)	33 (36.3)	17 (18.7)	8 (8.8)	8 (8.8)
Parietal	21 (100)	12 (57.1)	8 (38.1)	4 (19.0)	0
Occipital	10 (100)	4 (40.0)	4 (40.0)	0	0
Hemispherectomy	16 (100)	6 (37.5)	3 (18.8)	2 (12.5)	1 (6.2)
Multiple subpial transections	4 (100)	2 (50.0)	0	1 (25.0)	1 (25.0)
Corpus callosotomy	5 (100)	0	0	0	0
Total procedures	911 (100)	240 (26.3)	157 (17.2)	63 (6.9)	20 (2.2)
Procedure type					
Lesionectomy (Temporal and extratemporal)	118 (100)	26 (22)	16 (13.6)	8 (6.8)	2 (1.7)
Other	793 (100)	213(26.9)	141 (17.8)	54 (6.8)	18 (2.3)

Note: There were a total of 311 adverse events recorded in 240 procedures

*Total procedures with neurological adverse events = Neurological alone + Neurological and Surgical combined

Table 2: Neurological adverse events

Neurological adverse events	Total (n=911)					Temporal lobe procedure (n=764)					Extra Temporal lobe procedures (n=147)				
	Numbers	Persistent		Transient		Numbers	Persistent		Transient		Numbers	Persistent		Transient	
		E	*U*	E	U		E	U	E	U		E	U	E	U
Procedures with adverse events*	177 (19.4)	137 (15.0)	20 (2.2)	3 (0.3)	17 (1.9)	135 (17.7)	106 (13.9)	19 (2.5)	1 (0.1)	9 (1.2)	42 (28.6)	31 (21.1)	1 (0.7)	2 (1.4)	8 (5.4)
Quadrantanopia	85 (9.3)	77 (8.4)	6 (0.7)	2 (0.2)	0	80 (10.5)	72 (9.4)	6 (0.8)	2 (0.3)	0	5 (3.4)	5 (3.4)	0	0	0
Hemianopia	13 (1.4)	10 (1.1)	2 (0.2)	1 (0.1)	0	3 (0.4)	1 (0.1)	2 (0.3)	0	0	10 (6.8)	9 (6.1)	1 (0.7)	0	0
Hemiparesis/ Sensory loss	27 (3.0)	5 (0.5)	9 (1.0)	6 (0.7)	7 (0.8)	10 (1.3)	1 (0.1)	6 (0.8)	0	3 (0.4)	17 (11.6)	4 (2.7)	6 (4.1)	3 (2.0)	4 (2.7)
Monoparesis/ Sensory loss	9 (1.0)	6 (0.7)	0	1 (0.1)	2 (0.2)	1 (0.1)	0	0	0	1 (0.1)	8 (5.4)	6 (4.1)	1 (0.7)	0	1 (0.7)
Dysphasia	36 (4.0)	6 (0.7)	10 (1.1)	17 (1.9)	3 (0.3)	25 (3.3)	3 (0.4)	10 (1.3)	11 (1.4)	1 (0.1)	11 (7.5)	3 (2.0)	6 (4.1)	0	2 (1.4)
Frontalis weakness	28 (3.1)	19 (2.1)	2 (0.2)	6 (0.7)	1(0.1)	27 (3.5)	19 (2.5)	2 (0.3)	5(0.6)	1 (0.1)	1 (0.7)	0	1 (0.7)	0	0
Oculomotor	7 (0.8)	2 (0.2)	1 (0.1)	3 (0.3)	1 (0.1)	6 (0.8)	2 (0.3)	0	3 (0.4)	1 (0.1)	1 (0.7)	0	0	1 (0.7)	0

*One procedure may give in to >1 adverse event
Legend: E; expected U=unexpected

Table 3: Surgical adverse events

Surgical adverse events	Total (n=911)	Temporal lobe procedure				Without IC* (n=668)	Extra temporal lobe procedure				Without IC* (n=75)
		With IC* (n=96)					With IC* (n=72)				
		SD alone	Combination	SEEG alone	Total		SD alone	Combination	SEEG alone	Total	
CSF Leak (needing resuture)	11 (1.2)	0	1 (1.0)	0	1 (1.0)	8 (1.2)	0	0	0	0	2 (2.7)
DVT	1 (0.1)	0	0	0	0	0	0	0	0	0	1 (1.3)
Infection-Superficial surgical site	35 (3.8)	1 (1.0)	2 (2.1)	1 (1.0)	4 (4.2)	26 (3.9)	0	2 (2.8)	0	2 (2.8)	3 (4.0)
Infection-intracranial	8 (0.9)	0	1 (1.0)	0	1 (1.0)	5 (0.8)	0	0	0	0	2 (2.7)
Infection-Bone flap removed	24 (2.6)	0	3 (3.1)	1 (1.0)	4 (4.2)	6 (0.9)	3 (4.2)	7 (9.7)	0	10 (13.9)	4 (5.3)
Infection – other sites	5 (0.5)	0	0	0	0 (0)	4 (0.6)	0	0	0	0	1 (1.3)
Haematoma	3 (0.3)	0	0	0	0 (0)	2 (0.3)	0	0	0	0	1 (1.3)
Hydrocephalus	3 (0.3)	0	0	0	0 (0)	2 (0.3)	0	0	0	0	1 (1.3)
Headache	16 (1.8)	0	1 (1.0)	0	1 (1.0)	14 (2.1)	0	1 (1.4)	0	1 (1.4)	0

Notes: *IC indicates “Intracranial Monitoring”, SD= Subdural grid, SEEG= Stereo EEG

1. Procedures which underwent intracranial monitoring (IC) total =168 (temporal =96; extratemporal=72) and procedures which had not undergone IC =743 (temporal =668; extratemporal=75)

Table 4 –Analysis of persistent neurological adverse events in 5 year epochs

Years	Total number of operations	Temporal	Extra –temporal	*IC	Persistent neurological adverse events	
					Unexpected	Expected
1990 – 1994	116	99 (85.3%)	17(14.7%)	9 (7.8%)	5 (4.3%)	20 (17.2%)
1995 – 1999	222	195 (87.8%)	27 (12.2%)	25 (11.3%)	4 (1.8%)	18 (8.1%)
2000 – 2004	176	150 (85.2%)	26 (14.8%)	28 (15.9%)	1 (0.6%)	12 (6.8%)
2005 – 2009	205	181 (88.3%)	24 (11.7%)	39 (19%)	10 (4.9%)	28 (13.7%)
2010 – 2014	192	139 (72.4%)	53 (27.6%)	67 (34.9%)	6 (3.1%)	29 (15.1%)
Total	911	764 (83.9%)	147 (16.1%)	168 (18.4%)	26 (2.9%)	107 (11.7%)

***IC – individuals who have undergone intra-cranial monitoring in 5-year epochs**

Figure 1 – Categories of adverse events

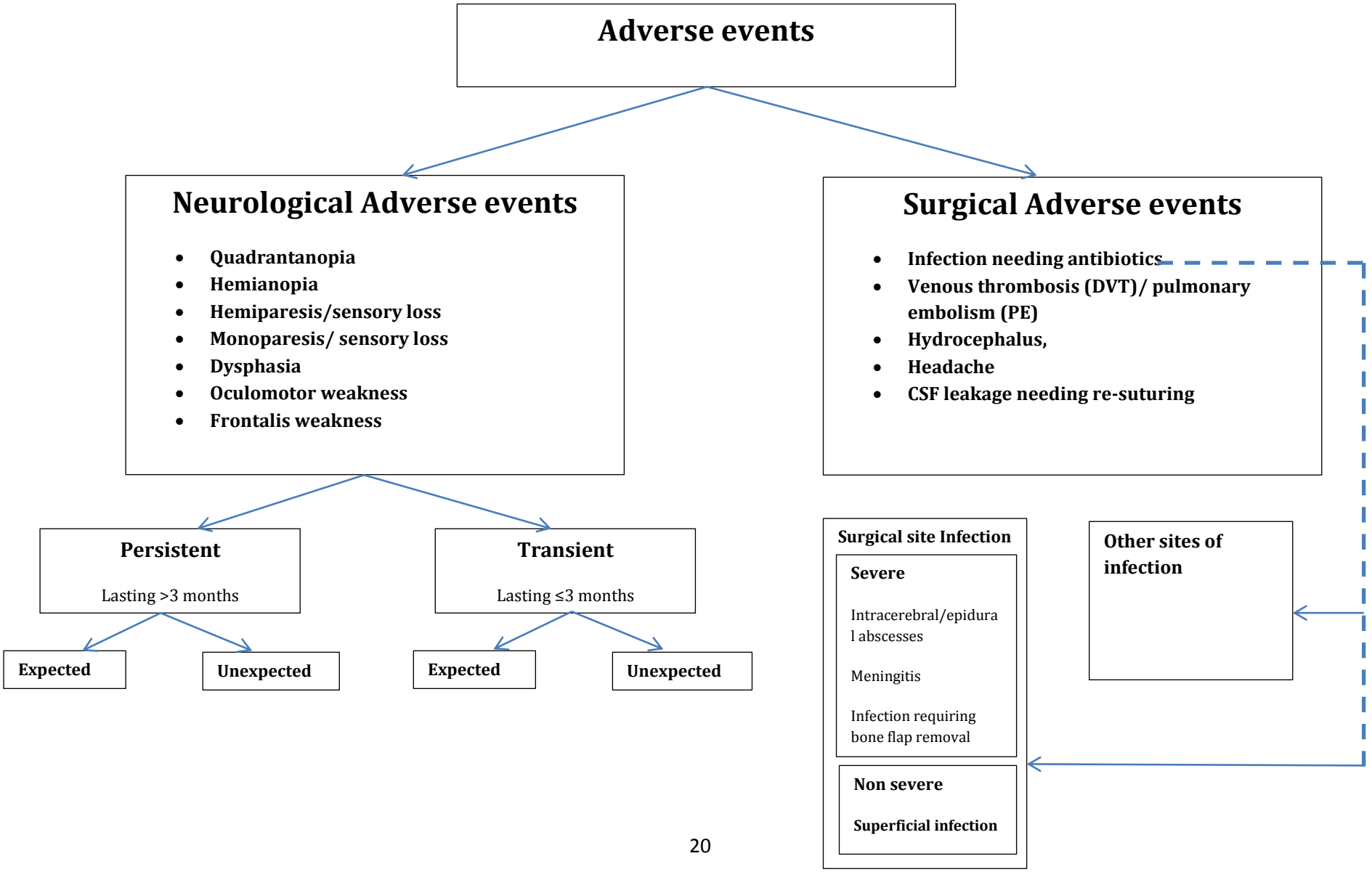

Figure 2 - Flow chart depicting procedures with adverse events