Reasons for not having epilepsy surgery

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Summary

Objective

To determine reasons for adults with drug-resistant focal epilepsy who undergo pre-surgical evaluation not proceeding with surgery, and identify predictors of this course.

Methods

We retrospectively analyzed data on 617 consecutive individuals at a tertiary referral center evaluated for epilepsy surgery between January 2015 and December 2019. We compared the characteristics of those in whom a decision not to proceed with surgical treatment was made with those who underwent definitive surgery in the same period. Multivariable logistic regression was performed to identify predictors of not proceeding with surgery.

Results

A decision not to proceed with surgery was reached in 315 (51%) of 617 individuals evaluated. Common reasons for this were an inability to localize the epileptogenic zone (n=104) or the presence of multifocal epilepsy (n=74). An individual choice not to proceed with intracranial EEG (n=50) or surgery (n=39), risk of significant deficit (n=33), declining non-invasive investigation (n=12), and co-existing neurological comorbidity (n=3) accounted for the remainder. Compared to 166 surgically treated, those who did not proceed to surgery were more likely to have a learning disability (OR: 2.35; 95% CI 1.07–5.16), normal MRI (OR: 4.48; 95% CI 1.68 to 11.94), extratemporal epilepsy (OR: 2.93; 95% CI 1.82–4.71), bilateral seizure onset zones (OR 3.05; 95% CI 1.41–6.61) and to live in more deprived socioeconomic areas (median deprivation decile 40-50% vs 50-60%, $p<0.05$).

Significance

Approximately half of those evaluated for surgical treatment of drug-resistant focal epilepsy do not proceed to surgery. Early consideration and discussion of the likelihood of surgical suitability or need for intracranial EEG may help direct referral for pre-surgical evaluation.

Keywords: Pre-surgical evaluation, socioeconomic deprivation, MDT, outcome

REASONS FOR NOT HAVING EPILEPSY SURGERY

INTRODUCTION

Surgery for selected people with drug-resistant focal epilepsy gives a greater chance of seizure freedom than medical therapy. [1, 2] Candidates for epilepsy surgery require a detailed pre-surgical evaluation to determine whether potentially curative surgery is feasible. This is extensive and time-consuming, requiring multimodal investigations and input from an experienced multidisciplinary team. [3] The whole process is costly but cost-effective if the outcome is seizure freedom. [4, 5]

In people with concordant semiology, EEG data and a neuroimaging abnormality, the chance of postoperative seizure freedom can be accurately predicted. [6] When this is not the case, additional information from fluoro-deoxyglucose positron emission tomography (FDG-PET), ictal single photon emission computed tomography (ictal SPECT), and intracranial EEG (icEEG) monitoring may be required, which entail additional time and healthcare costs. A recent report concluded pre-surgical evaluation was cost-effective even if the chance of proceeding to surgery was 5%. [5] This did not, however, include individuals with extratemporal epilepsy or the need for icEEG studies, which are both factors associated with lower surgical suitability. [7]

Guidelines suggest referring all people with drug-resistant focal epilepsy to an epilepsy surgery center; but realistic expectations of a favorable outcome, need for icEEG and risks of surgery should be discussed at the outset. The average time between the initial review to surgery has been reported between 56 and 183 weeks, highlighting the lengthy evaluation and the need to streamline pre-surgical assessment. [8, 9] While epilepsy surgery may be underutilized, up to two-

thirds of people referred with drug-resistant focal epilepsy do not ultimately proceed to surgical resection. [10-12]

Providing individuals with an early indication of their surgical suitability may help to focus on pre-surgical evaluation better. A previous evaluation at our center of 612 people admitted for pre-surgical video-telemetry between 2007 and 2012 found that the majority did not proceed to surgery. [10] A third of those who were offered surgery decided against proceeding. We aimed to determine the current situation at our center and characterize the demographics and clinical features of those who undergo pre-surgical evaluation but do not proceed to surgery. By comparing these characteristics with those of individuals who underwent surgery, we sought to identify factors that could predict the decision not to proceed.

METHODS

Study design and selection process

We retrospectively reviewed data from consecutive individuals discussed at weekly pre-surgical multidisciplinary team (MDT) meetings from 01 January 2015 to 31 December 2019. Individuals were referred to our center by neurologists for consideration of epilepsy surgery. Clinical history, examination, MRI brain, video-EEG telemetry, neuropsychological and neuropsychiatric evaluations, and in selected cases FDG-PET, ictal SPECT and icEEG recordings, were reviewed and discussed at this MDT meeting. Following the discussion, one of three possible consensus decisions was made:

a) Recommendation for surgery
b) Recommendation for further investigation
c) Recommendation not to proceed with surgery

We included those in whom the MDT decision was not to proceed with surgery. We also included those who were initially recommended for surgery or further investigation, but the clinical team or individual subsequently decided not to proceed. For comparison, we also evaluated those who underwent definitive surgery over the same 5-year period at the same site. A number of individuals in this latter group may have been discussed by the MDT before Jan 2015 (Figure 1).

We assessed demographic and clinical features, focusing on those characteristics often known before investigations with long waiting times, such as scalp video-EEG telemetry, ictal SPECT and icEEG recordings. The socioeconomic status of the individuals, who mostly lived in England, was assessed through the Index of Multiple Deprivation, which estimates relative deprivation levels among 32,844 areas of England, each containing approximately 1,500 residents. This index measures the relative deprivation in each area and is based on seven domains: income, employment, education/skills, health deprivation or disability, crime, barriers to housing and living environment deprivation. [13]

Standard protocol approvals, registration and consents

This study was approved as part of an ongoing epilepsy surgery audit at University College London Hospitals (registration number 45-202021-SE). As a service evaluation posing no risk, individual informed consent was not required.

Data analysis

We compared demographic, clinical, imaging and EEG findings between individuals who did not proceed to surgery and those who had surgery. We used a Pearson's Chi-Square test for dichotomous data and a Mann-Whitney U-test for continuous data, in each case, to test the null hypothesis of no association between the outcome of interest and the decision whether or not to

proceed with surgery. Odds ratios for binary outcomes were estimated using univariable logistic regression. Significant factors on univariable analysis were entered into a multivariable binary logistic regression to assess predictors of not proceeding to epilepsy surgery with a p-value <0.05 deemed statistically significant. We estimated odds ratios and associated 95% confidence intervals for individuals with combinations of demographic, imaging and electroclinical data not proceeding with surgery. Predicted probabilities of surgery were estimated from the fitted logistic regression model with associated 95% confidence intervals. We used IBM SPSS Statistics for Windows v20 (International Business Machines Corp, Armonk, NY) for data analysis.

RESULTS

A total of 617 individuals were discussed at the epilepsy surgery MDT meeting over the five years between 01 January 2015 and 31 December 2019. Of these, a definitive decision not to proceed, either at the MDT meeting or subsequently, was made in 315 people (Figure 1).

Individuals were evenly distributed by gender, and the median duration of epilepsy was 21 (range 1-65) years. Fifty-one (16%) had a learning disability, and 110 (35%) had a significant psychiatric diagnosis such as major depression, psychosis, severe anxiety, or a history of dissociative seizures.

The baseline clinical characteristics and investigatory data are summarized in Table 1. Comparable data for 166 individuals who underwent definitive epilepsy surgery over the same period is also provided. Fifty-six of these had pre-surgical evaluation before January 2015 (Figure 1).

Of the 315 individuals in whom a decision not to proceed with surgery was made, MRI was available in 314 (one had metal fragments in his skull, precluding MRI). Imaging showed a significant pathology in 172 (55%), with 30 (10%) having bilateral pathology. Bilateral MRI pathology (OR: 0.50; 95% CI 0.21-1.20) was not significantly more common in those who did not have surgery. There were differences in radiological features between the operated and non-operated cohorts. Those with a normal MRI or imaging evidence of gliosis were less likely to proceed to surgery. Conversely, those who proceeded to surgery had greater odds of having hippocampal sclerosis, focal cortical dysplasia, a cavernoma or a dysembryoplastic neuroepithelial tumour (DNT) on MRI (Table 2).

Of the 481 individuals included for analysis (166 who had surgery, 315 who did not proceed), all individuals had scalp video-EEG telemetry (n=478) or prolonged ambulatory EEG (n=3). Bilateral seizure onsets on ictal video telemetry was a strong predictor for not proceeding to surgery (OR: 3.05; 95% CI 1.41 to 6.61). In cases in whom surgery was performed despite this finding (n=10), this was because seizures from one hemisphere were thought to be subclinical (n=8) or subsequent icEEG demonstrated unifocal seizure onset (n=2). Bilateral interictal epileptiform discharges (OR 1.11; 95% CI 0.69-1.80) were not significantly more common in those who did not have surgery.

Fluorodeoxygenase PET scan was performed in 186 (59%) people within the group who did not proceed to surgery (Supplementary table 1). A higher proportion of those who did not proceed to have surgery had FDG-PET scans (OR: 2.78; 95% CI 1.48 to 5.19), likely reflecting the larger number of non-lesional cases in this cohort. Combining MRI and FDG-PET data showed that while 16/166 (10%) of those who had a resection had a normal MRI scan, and 13/166 (8%) had a normal FDG-PET scan, only 5/166 (3%) had normal MRI and FDG-PET scans, compared with 51/315 (16%) in the group who did not proceed to surgery (OR: 5.62;

95% CI 1.96 to 16.08). Individuals were less likely to be declined if they had an abnormal PET (OR: 1.89; 95% CI 1.25 to 2.85).

An ictal SPECT was performed in 17 (10%) surgical cases and in 51 (16%) of those who did not proceed to surgery. Individuals were less likely to be declined if they had focal changes on ictal SPECT (OR: 2.34; 95% CI 1.38 to 3.95).

Seventy-six individuals between both groups had icEEG (65 SEEG, 11 subdural grids). Of these, 48 (63%) proceeded to resection and 28 (37%) did not proceed. In these cases, reasons for not offering a resection were evenly distributed between ictal onset not adequately localized following icEEG (n=8; 29%), evidence of multifocality (n=7; 25%), subject declined a resection (n=7; 25%) and seizure onset in or adjacent to an eloquent cortex area (n=6; 21%).

We entered significant explanatory variables into a multivariable logistic regression model to further explore associations with proceeding to surgery and confirmed that those with a learning disability (OR: 2.35; 95% CI 1.07 to 5.16), extratemporal epilepsy (OR: 2.93; 95% CI 1.82-4.71), evidence of bilateral seizure onsets on an ictal recording (OR 3.05; 95% CI 1.41 to 6.61) and a normal MRI (OR: 4.48; 95% CI 1.68 to 11.94) were more likely not to proceed with surgery.

Different combinations of these four factors together could help predict the likelihood of individuals proceeding to surgery (Supplementary Table 2). Those with normal MRI and extratemporal epilepsy were much less likely to have surgery (OR: 8.71; 95% CI 3.89 to 19.53), as were those with a combination of extratemporal epilepsy and learning disability (OR: 3.76; 95% CI 1.56 to 9.66) or bilateral seizure onsets (OR: 4.25; 95% CI 1.68 to 10.72). The estimated probability of someone with none of these factors having surgery was 61.9% (95%

CI 54.8% to 68.4%). Conversely, the likelihood of those with a normal MRI together with a learning disability, bilateral seizure onset or extratemporal epilepsy proceeding to surgery was under 10% (Table 3).

Socio-economic status

We compared the Index of Multiple Deprivation at the time of evaluation of those who did not proceed to surgery to those who did. The median decile of deprivation was higher in those who did not proceed (median decile of deprivation 40-50% vs 50-60%, $p<0.05$), indicating that these people came from deprived areas (Figure 2).

Status at time of reporting

Of the 166 individuals who had definitive epilepsy surgery between 01 January 2015 and 31 December 2019, the median time from the first pre-surgical clinic appointment to surgery was 135 weeks (IQR 94-213 weeks). Of the 617 individuals discussed at pre-surgical MDT, 46 (7%) remain on the waiting list for surgery (as of January 2021), 139 (23%) are awaiting further investigation or icEEG, and seven (1%) died while still under evaluation, with five deaths deemed to be a direct consequence of seizures.

Reasons for not proceeding with surgery

There were a number of reasons why individuals did not proceed to surgery following pre-surgical evaluation (Figure 3).

The most common reason for not proceeding was an inability to localize the epileptogenic zone (n=104; 33%). In 96 of these cases the non-invasive electroclinical data including ictal recordings on scalp EEG did not provide sufficient lateralizing or localizing information to generate a hypothesis for the seizure onset zone. In the remaining eight cases, individuals

proceeded to icEEG however ictal patterns had a widespread distribution implicating widespread epileptic networks, and a single focus could not be adequately identified.

Other reasons for not proceeding to surgery included multifocal epilepsy (n=74; 23%), decision by the individuals not to proceed with icEEG (n=50; 16%), declining surgery (n=39; 12%), risk of significant deficit (n=33; 11%), declining further non-invasive investigations (n=12; 4%), or coexisting neurological co-morbidity (n=3; 1%).

In the 33 individuals in whom surgery was not performed due to the risk of a postoperative deficit, the concern was of affecting motor function (n=8; 3%), language (n=6; 2%), memory (n=6; 2%), vision (n=4; 1%) or other neuropsychological domains (Figure 3).

The decision not to proceed with surgery was made at different time-points of the pre-surgical evaluation pathway (Figure 4). In most, this was made at the MDT meeting (n=185; 59%) following review of phase I investigations, 16% after offering icEEG and 12% after offering surgery.

DISCUSSION

There are several reasons why those who are evaluated for epilepsy surgery do not proceed. Some individuals are considered unsuitable following pre-surgical evaluation, whereas others decline due to low odds of seizure freedom or concern over surgical risks. An early, realistic discussion surrounding the likelihood of surgery or the need for invasive icEEG monitoring may help inform individuals in deciding whether to undergo pre-surgical evaluation.

We investigated the predictive value of basic demographic data and non-invasive investigations in assessing the likelihood of having epilepsy surgery. Learning disability, normal MRI scan,

extratemporal epilepsy and bilateral seizure onset on video-EEG telemetry were all independent predictors of not proceeding to surgery on multivariable analysis. Combining demographic, imaging and EEG data improved the ability to predict the likelihood of not proceeding to surgery.

Our data add to several models designed to improve the selection of people for pre-surgical evaluation and ultimately resective surgery. [14, 15] A recent Epilepsy Surgery Grading Scale (ESGS) based on expert consensus opinion used basic information to assess the likelihood of proceeding to surgery and having a favorable outcome. [14] Stratification into different grades of the ESGS could predict the likelihood of surgery between 61.5% and 14.7%. Our study gives concordant results in a different center and adds weight to these findings. The estimated probability in our cohort of someone with a normal MRI together with a learning disability, bilateral seizure onset or extratemporal epilepsy proceeding to surgery was under 10%.

Individuals should be carefully advised on the probability of surgical feasibility and of the optimal chances of seizure remission and inevitable risks of surgery at the outset. In many cases, this discussion can occur even before being referred for investigations with high demand and long waiting times such as video-EEG telemetry, ictal SPECT or icEEG recordings. This will reduce the number of those who are thought suitable for icEEG or surgery but who decide not to proceed. At our center, over 70% of those who proceeded to icEEG were thought to be suitable surgical candidates, which is slightly higher than previously reported. [12] This highlights the utility of invasive recordings in further defining the seizure onset zone following non-invasive video-EEG telemetry.

Those who did not proceed to surgery had a threefold higher chance of having bilateral seizure onset on video-EEG telemetry. In those who subsequently had surgery, seizures from one

hemisphere were thought to be subclinical or electroclinical findings following scalp or icEEG were consistent with unifocal epilepsy. Previous studies have suggested approximately a third of people with unilateral TLE have bitemporal interictal epileptiform abnormalities. [16] Most cases with bitemporal interictal changes on scalp EEG have seizures that originate from one temporal lobe. [17, 18] Surgery for selected individuals with bitemporal epileptiform abnormalities but unilateral seizure onset on icEEG can still have good outcomes, with up to 40% seizure freedom. In people with bilateral seizure onset zones, surgery is not as favorable (12% seizure freedom). [18, 19]

With regard to phase II investigations, an FDG-PET was performed in a more significant proportion of people who did not have surgery, reflecting the higher number of non-lesional cases and searching for a focus. One-third of individuals with a normal MRI scan had an abnormal PET scan. Those who did not have surgery were over five times more likely to have had a normal MRI and normal FDG-PET, highlighting the utility of PET in determining surgical suitability for those with normal MRI. This is consistent with other reports that concordance between clinical consensus and FDG-PET can aid the decision to proceed with icEEG monitoring and possible surgery. [20]

Ictal SPECT is generally carried out as a prelude to icEEG to refine the strategy for placing intracranial electrodes. Less than half of those with an ictal SPECT proceeded to intracranial recording, as many individuals subsequently declined icEEG once it was offered. This stresses the importance of informing individuals adequately on the purpose of ictal SPECT before it is undertaken. Ictal SPECT is a time and resource-intensive investigation with radiation exposure. [21] Concordance between clinical consensus and ictal SPECT is a good predictor of surgical outcome. [20, 22]

Consistent with previous reports, the main reasons for not proceeding to surgery in our cohort were an inability to define the epileptogenic zone, presence of multiple foci or the individual/caregiver declining an operation. [12, 23] This decision was often made at the MDT meeting following a review of phase I investigations. Ictal video telemetry was a critical factor in deciding not to proceed. It was also a major determinant in guiding referral for phase II investigations such as FDG-PET, ictal SPECT or intracranial monitoring. Risk of a postsurgical deficit accounted for only a small proportion of people being unsuitable for surgery. Functional MRI to determine language dominance and baseline neuropsychology and neuropsychiatry assessments were all factors that influenced this reason not to proceed. Only 1% of people were rejected based on concurrent comorbidity at our center, reflecting referral selection at initial review in outpatient clinics.

A substantial number of people decided not to proceed after being offered icEEG or surgical resection comparable to reports from other centers, where up to a third of people or caregivers declined a resection. [11, 12, 23] In a minority of cases, this was because seizure control had improved. Compared to a previous audit of 2007-2012 at our center in which about a third of those offered surgery declined to proceed, in the current study, this was 12%, suggesting that selection for pre-surgical evaluation and advice given has improved. [10] Nonetheless, this finding emphasizes the critical importance of clearly describing the risks and benefits of surgery at the outset before embarking on investigations. This would also help avoid situations wherein, at the end of a complex process, the individual declines to proceed when the risk/benefit ratio may have been evident at the start of the process.

For example, in an individual with hippocampal sclerosis and concordant clinical and EEG data, there is an 80% chance of remission greater than one year, a 40% chance of long-lasting seizure freedom and 70% of individuals choose to remain on anti-seizure medication. [6, 24] There

is a 30-50% chance of significant decline in verbal memory and word-finding ability in a speech-dominant hemisphere, a 5-10% risk of a visual field defect that precludes driving and a 1% risk of severe morbidity from surgery such as hemiparesis. [24] This needs to be weighed against a 1% annual risk of fatality with continued seizures and 2% chance of remission with anti-seizure medication, if four have already been tried. [6, 24] For those with normal MRI and history of focal to bilateral tonic-clonic seizures in addition to a learning disability or extratemporal epilepsy, the chance of seizure freedom five years after surgery is less than 10%. [24]

Realistic odds of a good outcome should be conveyed to individuals throughout the entire process. Advising people of the likely chance of seizure remission and the inevitable risks of surgery is appropriate at the outset. If they do not find these acceptable, there is little merit in subjecting them to a full evaluation. Compared to our previous audit, rates of people declining intracranial recording or surgery once it is offered have dropped substantially, likely due to our efforts at improved counseling throughout the pre-surgical evaluation.

We also investigated whether socioeconomic deprivation was more severe among those with drug-resistant epilepsy who do not end up having epilepsy surgery compared to those that do. This could highlight groups in society where further efforts should be made to help facilitate access to epilepsy surgery. There was a significant difference in the distribution of deprivation deciles, with people who did not have epilepsy surgery residing in more deprived areas. Whether socioeconomic deprivation is a cause or consequence of not proceeding to epilepsy surgery is unclear, though the impact that poor seizure control has on work capability, driving status and employment has been well established. [25-27] Accessing appropriate services can be challenging for those without private health insurance, and many adults with epilepsy struggle to afford important elements of health care, including medication. [28] Even with free at the point

of delivery healthcare provision, pre-surgical evaluation is demanding in terms of repeated visits to the center, with associated costs and need for support that may not be readily available for those living with a degree of deprivation. While the UK National Health Service aspires to provide equal access to healthcare, our findings suggest it does not fully compensate for social deprivation, as deprived people may be less likely to stay the course. It also raises the possibility that low uptake of surgery in socially deprived areas may be a mechanism by which health inequality is maintained.

The cost-effectiveness of surgery, particularly for those who achieve seizure freedom with anterior temporal lobectomy has been well established. [29, 30] Data on the cost-effectiveness of the pre-surgical evaluation itself, however, particularly when over 50% of individuals assessed do not have surgery, is much less clear. Intracranial monitoring requires expertise in the implantation of electrodes and interpretation of these results but comes with associated costs related to the antecedent non-invasive investigation, the need for the additional operating room, nursing and neurophysiology staff, and admission to a video-EEG telemetry unit. We support guidelines recommending early referral for consideration of epilepsy surgery in those with drug-resistant focal epilepsy. This should, however, be tempered by realistic expectations of surgical suitability, which must be conveyed to individuals and their families early in the process.

There were strengths and limitations of our study. This was a retrospective analysis of a prospectively followed cohort of adults investigated at a single tertiary referral center. As our cohort consisted only of people who had been discussed in a pre-surgical MDT meeting, there was also a selection bias with those thought unsuitable for surgery following initial clinic consultation not included in the analysis. Pre-surgical advice to people at our center routinely includes discussing the likelihood of seizure freedom, as assessed by current literature.

Inevitably, this could reduce the possibility of individuals with specific characteristics, such as normal MRI, proceeding to surgery and introduce a bias to our findings. Nonetheless, our results reflect real-world experience of an epilepsy surgery center in a developed country with free at the point of delivery healthcare and describe the likelihood of these individuals proceeding with evaluation or surgery following counseling. It would be of great interest to obtain comparative data from other Epilepsy Surgery Centers.

In keeping with the intention to treat methodology, we included the minority of people offered surgery but who declined an operation in our multivariate analysis. This could have reduced the impact of significant findings, as it is likely some of these individuals had a more favorable pre-surgical evaluation. Our assessment of socioeconomic status was also limited to the Index of Multiple Deprivation. While this is frequently used to approximate socioeconomic status in England, it does not take into account individual variations or those who reside in other areas of the UK or overseas.

CONCLUSION

We have identified how combinations of demographic, clinical, and investigatory data can help predict whether people with drug-resistant focal epilepsy are likely to proceed to surgery. Learning disability, a normal MRI or FDG-PET scan, extratemporal origin and bilateral seizure onset zones on scalp-EEG are associated with lower surgical suitability. Discussing these results and their implications may help clinicians and individuals decide whether to undergo the expensive, time-consuming and sometimes invasive pre-surgical evaluation.

KEY POINTS

- Many people with drug-resistant epilepsy who are referred for surgery do not proceed to an operation despite lengthy pre-surgical evaluation.

- Inability to localize the epileptogenic zone, multifocal epilepsy, and declining icEEG or an operation are the main reasons why people do not proceed.

- Combinations of clinical and investigatory data can predict likelihood of having surgery and should be discussed with individuals early in the referral pathway.

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Figure and Table Legend

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Table 1: Baseline characteristics of individuals discussed in the Queen Square Pre-Surgical MDT and did or did not have surgery from Jan 2015 - Dec 2019

	Not for surgery (n=315)	**Had surgery (n=166)**	**Odds Ratio (95% CI)**	**P value**
Demographics				
Women, n/N (%)	157/315 (50)	80/166 (48)	1.07 (0.73-1.56)	0.73
Age of epilepsy onset, median (IQR), y	12 (7-18)	15 (7-23)	**0.98 (0.96-1.00)**	**0.014**
Age at final decision [a], median (IQR), y	36 (28-44)	38 (30-48)	0.99 (0.97-1.00)	0.06
Learning disability, n/N(%)	51/315 (16)	10/166 (6)	**3.01 (1.49-6.11)**	**<0.001**
History of febrile convulsions, n/N (%)	36/315 (11)	27/166 (16)	0.64 (0.37-1.09)	0.34
Prolonged early childhood convulsion, n/N (%)	17/315 (5)	16/166 (10)	0.54 (0.26-1.09)	0.08
Previous significant head trauma, n/N (%)	21/315 (7)	9/166 (5)	1.25 (0.56-2.79)	0.59
Psychiatric diagnosis, n/N (%)	110/315 (35)	72/166 (43)	0.69 (0.47-1.02)	0.10
Prior neurological insult				
Meningitis/encephalitis, n/N (%)	18/315 (5)	8/166 (5)	1.20 (0.51-2.81)	0.68
Previous stroke, n/N (%)	7/315 (2)	6/166 (2)	1.06 (0.26-4.27)	0.76
Previous brain surgery, n/N (%)	19/315 (6)	11/166 (7)	0.96 (0.45-2.05)	0.99
Epilepsy features				
Duration of epilepsy, median (IQR), y	21 (12-31)	22 (10-33)	1.01 (0.99-1.02)	0.62
History of generalized sz, n/N (%)	228/315 (72)	131/166 (79)	0.70 (0.45-1.10)	0.12
Focal unaware sz/month, median (IQR)	8 (2.5-23)	6 (2.0-20)	1.00 (0.99-1.01)	0.07
Generalized sz/month, median (IQR)	0 (0-1)	0 (0-0.56)	1.01 (0.98-1.05)	0.13
Imaging characteristics				
Abnormal MRI, n/N (%)	172/315 (55)	150/166 (90)	**0.13 (0.07-0.23)**	**<0.001**
Bilateral MRI abnormality, n/N (%)	30/315 (10)	8/166 (5)	0.48 (0.22-1.07)	0.14
Video telemetry data				
Bilateral [b] epileptiform abnormality (interictal), n/N (%)	114/315 (36)	47/166 (28)	1.44 (0.95-2.16)	0.08
Bilateral [b] epileptiform abnormality (ictal), n/N (%)	72/315 (23)	10/166 (6)	**4.62 (2.32-9.23)**	**<0.001**
Extratemporal epilepsy, n/N (%)	190/315 (60)	43/166 (26)	**4.35 (2.87-6.58)**	**<0.001**

[a] Final decision not to have surgery or date of surgical procedure

[b] Inclusive of both synchronous and independently bilateral epileptiform abnormalities

Table 2: MRI features in those who did and did not have surgery				
Finding	**Not for surgery (n=315, %)**	**Had surgery (n=166, %)**	**Adjusted [a] OR (95% CI)**	**P Value**
Normal	142 (45)	16 (10)	4.48 (1.68-11.94)	**<0.001**
Gliosis	28 (9)	4 (2)	4.25 (1.38-13.11)	**0.013**
Polymicrogyria	5 (2)	0 (0)		
Encephalomalacia	20 (6)	5 (3)	1.81 (0.63-5.24)	0.27
Atrophy	13 (4)	3 (2)	1.59 (0.41-6.20)	0.50
Focal cortical dysplasia	17 (5)	16 (10)	0.21 (0.09-0.49)	**<0.001**
Hippocampal sclerosis	37 (12)	48 (29)	0.48 (0.28-0.84)	**0.018**
Cavernoma	7 (2)	16 (10)	0.17 (0.06-0.46)	**<0.001**
DNT	5 (2)	37 (22)	0.08 (0.03-0.21)	**<0.001**
Heterotopia	8 (2)	2 (1)	0.98 (0.18-5.25)	0.98
Other [b]	32 (11)	19 (11)		

[a] Adjusted for baseline characteristics, video-telemetry findings and presence of bilateral pathology.

[b] Including cases with mixed or indeterminate pathology

Table 3: Estimated probabilities of surgery for combinations of predictive factors					
Learning Disability?	**Normal MRI?**	**Bilateral seizure onset?**	**Extratemporal epilepsy?**	**Estimated Pr(Surgery)**	**95% Confidence Interval**
No	No	No	No	0.619	(0.548, 0.684)
Yes	No	No	No	0.407	(0.241, 0.599)
No	Yes	No	No	0.204	(0.127, 0.311)
No	No	Yes	No	0.345	(0.199, 0.528)
No	No	No	Yes	0.364	(0.277, 0.462)
Yes	Yes	No	No	0.098	(0.041, 0.217)
Yes	No	Yes	No	0.183	(0.072, 0.392)
Yes	No	No	Yes	0.196	(0.103, 0.340)
No	Yes	Yes	No	0.077	(0.033, 0.169)
No	Yes	No	Yes	0.083	(0.047, 0.142)
No	No	Yes	Yes	0.157	(0.082, 0.281)
Yes	Yes	Yes	No	0.034	(0.011, 0.103)
Yes	Yes	No	Yes	0.037	(0.015, 0.086)
Yes	No	Yes	Yes	0.073	(0.028, 0.176)
No	Yes	Yes	Yes	0.029	(0.012, 0.065)
Yes	Yes	Yes	Yes	0.012	(0.004, 0.037)

Table S1: Additional investigations prior to final decision not to proceed with epilepsy surgery		
	Not for surgery (n=315)	**Had surgery (n=166)**
FDG-PET scan, n/N (%)	186/315 (59)	45/166 (27)
Abnormal scan, n (%)	119/186 (64)	32/45 (71)
Normal scan, n (%)	67/186 (36)	13/45 (29)
Normal MRI & normal PET, n/N (%)	51/315 (16)	5/166 (3)
Ictal SPECT, n/N (%)	51/315 (16)	17/166 (10)
Bilateral abnormality, n (%)	5/51 (10)	1/17 (6)
Dominant involvement, n (%)	15/51 (29)	4/17 (24)
Non-dominant involvement, n (%)	28/51 (55)	7/17 (41)
No abnormality found, n (%)	3/51 (6)	5/17 (29)
icEEG recording, n/N (%)	28/315 (9)	48/166 (29)
Subdural strips, grids +/- depth electrodes	3/28 (11)	12/48 (25)
Stereo-EEG	25/28 (89)	36/48 (75)

Table S2: Multivariable predictors of not proceeding to epilepsy surgery				
Characteristic	**No surgery (n=315)**	**Had surgery (n=166)**	**Adjusted [a] OR (95% CI)**	**P value**
Learning disability, n/N (%)	51/315 (16)	10/166 (6)	2.35 (1.07-5.16)	**<0.001**
Learning disability & extratemporal epilepsy, n/N (%)	39/315 (12)	6/166 (4)	3.76 (1.46-9.66)	**0.003**
Learning disability & normal MRI, n/N (%)	18/315 (6)	1/166 (1)	8.10 (1.02-64.18)	**<0.05**
Bilateral interictal epileptiform abnormalities, n/N (%)	114/315 (36)	46/166 (28)	1.11 (0.69-1.80)	0.23
Extratemporal origin, n/N (%)	190/315 (60)	43/166 (26)	2.93 (1.82-4.71)	**<0.001**
Bilateral seizure onsets, n/N (%)	72/315 (23)	10/166 (6)	3.05 (1.41-6.61)	**0.002**
Normal MRI scan, n/N (%)	142 (45)	16 (10)	4.48 (1.68-11.94)	**<0.001**
Extratemporal origin & bilateral seizure onsets, n/N	53/315 (17)	6/166 (4)	4.25 (1.68-10.72)	**<0.001**
Normal MRI & extratemporal epilepsy, n/N (%)	95/315 (30)	7/166 (4)	8.71 (3.89-19.53)	**<0.001**
Normal MRI, bilateral interictal abnormalities & extratemporal epilepsy, n/N (%)	42/315 (13)	2/166 (1)	9.65 (2.27-40.95)	**<0.001**
[a] Adjusted for age, psychiatric comorbidity and frequency of seizures/month				