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Socioeconomic outcome of epilepsy surgery: A controlled national study

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ABSTRACT

Purpose: Epilepsy surgery has been a standard treatment for refractory epilepsies that cannot be controlled by standard medical treatment. We aimed to evaluate the health and social consequences of resective surgery relative to controls from a study of national data.
Methods: Using the Danish National Patient Registry we identified all subjects with an epilepsy diagnosis between 1996 and 2009 and compared them with a group of patients with an epilepsy diagnosis who had had neither epilepsy surgery nor a vagus stimulation diagnosis by the index date, and who were matched by gender, index year for epilepsy diagnosis, and index year for epilepsy surgery. We considered all the health and social information available in the Danish health, medication and social registers. The duration of follow-up was three years.
Results: 254 epilepsy patients and 989 controls were analyzed. Surgery patients were more severely affected by their disease as indicated by health care use and social impact before the surgical procedure. Patients who underwent epilepsy surgery had a significantly lower costs associated with the use of medication, outpatient services, inpatient admissions, and accident and emergency visits after surgery. The surgical intervention had no significant effects on social status in terms of occupation and educational level.
Conclusion: Although epilepsy surgery was followed by a reduction in inpatient and outpatient health care use, medication and use of accident and emergency facilities, suggesting a positive effect on the epileptic disease, there was no significant effect on social outcome measures.

1. Introduction

Epilepsy is a serious chronic neurological disorder affecting people of all ages [1]. The disease is strongly associated at all ages with significant morbidities, mortality, social stigma, educational and professional problems, and reduced quality of life. Epilepsy may thus have a substantial socioeconomic impact [2,3]. Resective epilepsy surgery has been a standard treatment for refractory epilepsies that cannot be controlled by standard medical treatment [4]. Epilepsy surgery has been shown to lead to less seizure activity in randomized clinical trials when compared with continued medical therapy [4], but its long-term cognitive, psychiatric, psychosocial, and quality-of-life outcomes have been less well described [5]. Epilepsy surgery is associated with positive but also potentially negative psychological and cognitive effects [6–10], for which reason there is a need for more research and supportive intervention [7]. A number of studies have addressed the social outcome of epilepsy surgery; in general, freedom from seizure tends to be a positive factor for outcome measures, but there is a lack of controlled trials and of evaluations of factual social outcome as determined by education and employment [7,9,11–13]. As such, a national estimate of social outcome compared with a control group has not previously been attempted. Recently, we described factual direct and indirect costs in child and adult patients diagnosed with epilepsy in Denmark [3], and showed that epilepsy

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is associated with a substantial burden not only at the time of diagnosis and after, but also before diagnoses in children and adults. The study showed substantial direct, health-related costs, which suggests high comorbidity in epilepsy patients. In this study, we focus on the social outcome for patients undergoing epilepsy surgery based on data from the national population.

In Denmark, information from general practice, public and private hospitals, social and educational status of all Danish citizens is registered in central databases and linked by a unique identification number. This makes it possible to identify subjects with epilepsy, and trace their health, educational, professional and income level, and subsequently to calculate direct and indirect costs related to diseases. We took advantage of historical medical archives of patients hospitalized with epilepsy in Denmark since 1998 and randomly selected a control group from the whole population, matched by age, gender and social background. We included detailed information for the entire Danish population obtained from nationwide registers, including that on education, employment, welfare benefits, family conditions, hospital contacts, visits to general practitioners and use of medication. Using these data enables the long-term health and social effects of the resective surgical procedure to be established.

2. Methods

The study is a matched case-control study in which we compare the case study group (epilepsy diagnosed and treated by surgery) and their control group (epilepsy diagnosed but not treated with surgery) 12 months before the index date (pre-surgery period) with a three-year follow-up after the index date (post-surgery period). The index date was taken as the date of epilepsy surgery.

2.1. Study population

The study includes only patients with an ICD-10 G40x epilepsy diagnosis or those categorized as G41X (status epilepticus).

We followed 268 patients who underwent epilepsy surgery at some point between 1 January 1996 and 31 December 2009, and 1056 controls. 254 epilepsy patients and 989 controls were alive three years after the index date (Table 1). In the analysis of cost and income three years after surgery we only included case patients and their controls who were alive three years after the index date (Table 1). The analyses of cost and income before the index date were based on the population alive two years after the index date. The study population at the index date was used only in the survival analysis (Tables 2A and 2B).

Table 1
Summary characteristics 3 years after temporal lobe surgery.

	Epilepsy surgery N = 254			Control N = 989			P
	N	%	Mean	N	%	Mean	
Age (years)							
0–19	68	26.8	31	269	27.2	31	
20–39	107	42.1		414	41.9		
40+	79	31.1		306	30.9		
Gender							
Male	131	51.6		509	51.5		
Female	123	48.4		480	48.5		
Years since diagnosis			12			12	
Education							
Primary	89	35.0		387	39.1		0.148
Secondary	15	5.9		47	4.8		
Vocational	60	23.6		235	23.8		
College	37	14.6		105	10.6		
Unknown	53	20.9		215	21.7		
Charlson							
Charlson Index			0.06			0.05	0.911

2.2. Case group

The epilepsy surgery case group consisted of all epilepsy patients who underwent epilepsy surgery (ICD code KAAJ) before or during the study period. We excluded patients who had undergone an operation for vagal nerve stimulation before the index date, which was taken to be the date a patient was first registered with an epilepsy surgery code in the Danish National Patient Register. Patients who underwent both vagal nerve stimulation and epilepsy surgery in the study period were excluded from the study.

2.3. Control group

The control group consisted of patients with an epilepsy diagnosis who had not had either epilepsy surgery or a vagus stimulation diagnosis by the index date. We matched the cases and controls with respect to gender, index year of epilepsy diagnosis, and index year of epilepsy surgery. We did not match with respect to medication at the time of diagnosis. Matching by year of epilepsy surgery as well as year of epilepsy diagnosis ensured that the control patients were alive at the time of surgery. We censored four patients and 11 controls who migrated into or out of the country during the period analyzed (pre- or post-surgery).

2.4. Health care costs

Health care costs were calculated as the yearly cost during the 12 months before, and in the two and three years after, the index date. The total costs were divided into outpatient, inpatient, accident and emergency, medicine and primary health sector costs and those directly related to epilepsy. The latter included all costs incurred by patients registered with an epilepsy diagnosis (code ICD-10 G40X or G41X) and those for epilepsy medication. Comorbidities were estimated using the Charlson Index [14] as described in Ref. [15].

Only patients who were eligible throughout the whole period were included in the analysis.

2.5. Income

Income is a stock variable (income by calendar year, e.g., income in 2011) so we could not follow patient income before and after the index date, as we were able to do with their health care costs.

We used income data from the calendar year before the index year, and those from one and two years thereafter. Patients younger than 18 years of age were excluded from the income calculation because of the absence or scarcity of information (for those younger than 15 and 18 years of age, respectively). 23% of those who had undergone epilepsy surgery were younger than 18 years of age at the time of their operation and were therefore excluded.

Health care costs and income are presented in Euros (€), adjusted to 2015 levels.

2.6. Method for comparison of cost and income

The significance of the cost and income estimates for the matched-case and control groups was assessed by non-parametric

Table 2A
Health care cost analysis at 3 years post-surgery.

	Pre-surgery period			Post-surgery period		
	Case	Control	P	Case	Control	P
N	254	989		254	989	
Cost	Mean (€)	Mean (€)		Mean (€)	Mean (€)	
All healthcare costs						
Outpatient services	646.0	289.3	<0.001	585.9	371.6	0.360
Inpatient admissions	4429.2	1579.9	<0.001	3339.3	1464.6	<0.001
Accident and emergency	83.8	49.6	<0.001	52.1	49.1	1.000
Prescription medicine	4152.5	853.2	<0.001	2709.8	873.8	<0.001
Primary health sector	301.3	337.9	0.980	438.9	369.1	0.810
Epilepsy-related health care costs						
Outpatient services	342.6	21.1	<0.001	85.2	10.8	<0.001
Inpatient admissions	3430.7	150.1	<0.001	1106.1	177.0	<0.001
Accident and emergency	22.7	4.8	<0.001	9.1	1.2	<0.001
Prescription medicine	3754.7	454.1	<0.001	2255.9	396.2	<0.001

Table 2B
Change in health care costs from pre-surgery to post-surgery period.

	Change in health care costs		
	Case	Control	P
N	254	989	
Cost	Mean (€)	Mean (€)	
All healthcare costs			
Outpatient services	−60.1	82.3	0.920
Inpatient admissions	−1090.0	−115.3	0.700
Accident and emergency	−31.7	−0.5	0.700
Prescription medicine	−1442.7	20.6	<0.001
Primary health sector	137.6	31.3	0.080
Epilepsy-related health care costs			
Outpatient services	−257.4	−10.2	<0.001
Inpatient admissions	−2324.6	26.9	<0.001
Accident and emergency	−13.6	−3.6	0.020
Prescription medicine	−1498.8	−57.9	<0.001

bootstrap t-test analysis because the data were not normally distributed.

To analyze the costs, a bootstrapped t-test was used to compare the incomes of the cases and controls, matching for age, gender and date of diagnosis. Educational level and comorbidity, which are summarized in the descriptive statistics, were not used as covariates in the comparative analysis of costs.

2.7. Occupation

We used the occupational status in the November of the year before the index year and in the November of years 2 and 3 after the index year.

3. Results

3.1. Descriptive

The characteristics of the sample at the index date for the population that was alive two years after epilepsy surgery are shown in Table 1. Note that the sample includes only patients alive in year 2 (see study design). The characteristics that were not matched were tested to see whether they differed significantly between the surgery and control groups using the chi-square test for discrete variables and the t-test for continuous variables.

Due to the small number of observations and the large number of children in the dataset, information about completed education was limited, so we confined our comparison to those with primary education vs. those with more than primary education. In the event, we found no differences in the proportions that underwent surgery between the two educational levels. The level of morbidity, as determined by the Charlson Index [15], was significantly higher in the surgical group than in the control group.

3.2. Health care costs

Patients who had undergone epilepsy surgery used more health care services before and after the surgical procedure than the controls (Tables 2A and 2B) as estimated from outpatient, inpatient, accident and emergency, medication and primary health sector costs and the costs related to the epilepsy diagnoses. Patients who underwent epilepsy surgery incurred significantly lower costs associated with use of medication, outpatient services, inpatient admissions and accident and emergency visits after their surgery (Table 2B).

In the comparisons of heath care costs, the bootstrapped t-test enabled comparison of cases and controls. Educational level and

Table 3A
Occupational status at 3 years pre- and post-surgery.

	Pre-surgery period					Post-period				
	Case		Control		P*	Case		Control		P*
N	254		989			254		988		
	N	%	N	%		N	%	N	%	
Occupational status					0.103					0.004
Disability pension	49	19.3	170	17.2		63	24.8	196	19.8	
Employed	105	41.3	472	47.7		97	38.2	475	48.1	
Unemployed and not in labor force	45	17.7	136	13.8		52	20.5	156	15.8	
Children <16 year	55	21.7	211	21.3		42	16.5	161	16.3	

Table 3B
Income analysis at 3 years pre and post-surgery.

	Pre-surgery period			Post-surgery period		
	Case	Control	P	Case	Control	P
N[a]	195	756		195	756	
Income	Mean (€)	Mean (€)		Mean (€)	Mean (€)	
Total income	32049.1	34235.9	0.170	34137.2	37248.6	0.044

Probabilities are those associated with chi-square tests.
[a] Income does not include the group of people aged 0–17 years.

comorbidity, which are shown in the descriptive statistics, were not considered in the cost analyses.

3.3. Occupational status and income

Table 3A shows the occupation status the year before the index year and two years thereafter. The difference in occupational status between adult cases and controls was examined with a chi-square test. Table 3B shows the average annual income for the cases and controls in the year before, and two years after, the index year.

Patients who underwent surgery had a lower employment rate and level of education compared with the controls. However, sub-analysis showed no significant differences relative to the non-surgical controls.

4. Discussion

In this national register study of patients who underwent epilepsy surgery, we found that, compared with a matched control group: (1) surgery patients were more severely affected by their disease in terms of health care use and social impact before the surgical procedure, (2) patients who underwent epilepsy surgery incurred significantly lower costs associated with the use of medication, outpatient services, inpatient admissions and accident and emergency visits after surgery, but (3) there were no significant effects on social status in terms of occupation and educational level of the surgical intervention.

For decades, resective epilepsy surgery has been the standard treatment for refractory focal epilepsies that cannot be controlled by standard medical treatment. We included all patients who underwent resective epilepsy surgery in the period. Detailed data from Danish epilepsy surgery patients have not been evaluated yet, but the population is very similar to the patient population that has undergone epilepsy surgery in Sweden. The same protocol is used. A recent Swedish paper clearly describes that temporal lobe resections account for more than 70% of the surgeries and that the majority of patients are younger adults [16]. Several reports have documented the effect of epilepsy surgery on seizure activity. Resection of the temporal lobe in particular has consistently shown the most positive effect, whereas extra-temporal resection has a weaker effect on seizure outcome measures [17]. The outcome as determined by psychological, familiar and social factors in case-based series has formerly been evaluated [10], but this was less clear in a controlled study [5]. Epilepsy surgery was associated with lower rates of seizure activity in randomized clinical trials than with continued medical therapy [4]. However, the consequences for long-term cognitive, psychiatric, psychosocial, and quality-of-life outcomes were less clear. Despite good outcomes from high-quality clinical trials, referrals of patients with seizures refractory to medical treatment remain infrequent [5]. We show that overall, although patients are more affected than comparable epilepsy patients, they benefit in terms of reduced use of medication, outpatient services, inpatient admissions, and accident and emergency visits after surgery. However, the overall social prognosis was not affected within the observation period. We believe that this effect shows that the patients' disease is diagnosed at a time when its consequences for social and educational aspects are already present. We have previously shown that that the health and social status of epilepsy patients is involved years before the diagnosis [3], which is why a major effect on social outcome may be limited by the intervention [11,18–20]. Although we cannot compare the diseases, other studies have shown stable (and decreasing) social effects after a period exceeding 2–5 years [3,21,22], which is why it is doubtful that the social outcome will change beyond this period, unless special social care and interventions are instigated. This was also the outcome of a Swedish study showing that a postsurgery rehabilitation program after temporal lobe surgery improved employment status [23].

Epilepsy is associated with significant morbidities because of underlying brain diseases and disease consequences related to the seizures. The current study shows that although epilepsy surgery may have a positive effect on seizure outcome, the effect on educational and social outcome is limited, despite the potential for reducing seizure frequency. Epilepsy is associated with long-term negative consequences [3], and it seems that the intervention should probably be performed earlier in the course of the disease [24], at a time when the social outcomes may be more amenable to modification. We cannot rule out the possibility that greater educational and social intervention is needed for this group of patients.

4.1. Limitations and strengths of the study

Although the study involved a relatively large sample of patients, the total follow-up time was limited. If we had used a longer follow-up period, there would have been fewer observations, which would have reduced the number of cases we could have included. We selected a control group matched by age, gender, geographical location and time of diagnosis, but not with respect to disease severity. A limitation of the NPR is that it does not provide information about seizure activity. It would be useful to determine whether early intervention after disease onset has any social or health benefits. The number of patients observed in this study and their wide range of ages limit such subgroup analysis. The strengths of this study are that it considers every epilepsy patient in Denmark who underwent surgery during the study period, and their corresponding educational and social information.

5. Conclusions

Patients who undergo epilepsy surgery are generally more affected by the disease than are controls matched by age, gender and time of surgery. Epilepsy surgery was followed by a reduction in health costs, as indicated by inpatient and outpatient care, use of accident and emergency services, and medication use, suggesting that it has a positive effect on the disease. However, there was no significant effect on social outcome measures as indicated by occupation.

Conflict of interest statement

None of the authors reports any conflict of interest.

Author contributions

Poul Jennum (PJ) and Jakob Kjellberg (JK): creation, initiation and management of the project. PJ is the main author. JK and RI

performed the statistical analyses and commented on the manuscript. JC and AS commented on the methods and critically revised the manuscript. All authors approved the final version of the manuscript.

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