Electroconvulsive therapy and risk of dementia in patients with affective disorders: a cohort study



Merete Osler, Maarten Pieter Rozing, Gunhild Tidemann Christensen, Per Kraqh Andersen, Martin Balslev Jørgensen

Summary

Background Electroconvulsive therapy (ECT) is the most effective treatment for severe episodes of mood disorders. Temporary memory loss is a common side-effect, but ongoing discussions exist regarding potential long-term adverse cognitive outcomes. Only a few studies have examined the frequency of dementia in patients after ECT. The aim of this study was to examine the association between ECT and risk of subsequent dementia in patients with a first-time hospital diagnosis of affective disorder.

Methods We did a cohort study of patients aged 10 years and older in Denmark with a first-time hospital contact for an affective disorder from Jan 1, 2005, through Dec 31, 2015, identified in the Danish National Patient Registry with ICD-10 codes F30.0 to F39.9. From the registry we retrieved information on all ECTs registered for patients and followed up patients for incidental dementia (defined by hospital discharge diagnoses or acetylcholinesterase inhibitor use) until Oct 31, 2016. We examined the association between ECT and dementia using Cox regression analyses with multiple adjustments and propensity-score matching on sociodemographic and clinical variables.

Findings Of 168 015 patients included in the study, 5901 (3.5%) patients had at least one ECT. During the median follow-up of 4.9 years (IQR 2.4-7.8) and 872 874 person years, the number of patients who developed dementia was 111 (0·1%) of 99 045 patients aged 10-49 years, 965 (2·7%) of 35 945 aged 50-69 years, and 4128 (12·5%) of 33 025 aged 70-108 years. 217 (3.6%) of the 5901 patients treated with ECT developed dementia, whereas of 162 114 patients not treated with ECT 4987 (3.1%) developed dementia. The corresponding incidences were 70.4 cases per 10000 personyears (95% CI 61.6-80.5) and 59.2 per 10000 person-years (57.6-60.8). In patients younger than 50 years and 50-69 years, ECT was not associated with a risk of dementia compared with age-matched patients who were not given ECT (age-adjusted hazard ratio [HR] 1.51, 95% CI 0.67-3.46, p=0.32; and 1.15, 0.91-1.47, p=0.22, respectively). In patients aged 70 years and older, ECT was associated with a decreased rate of dementia (0.68, 95% CI 0.58-0.80; p<0.0001), but in the propensity-score matched sample the HR was attenuated (0.77, 0.59-1.00; p=0.062). 31754 patients (17.6%) died during follow-up (mortality rate per 1000 person-years 35.7, 95% CI 35.3-36.2) and supplementary analyses suggested that the risk of dementia, taking the competing mortality risk into account, was not significantly associated with ECT (subdistribution HR 0.98, 95% CI 0.76-1.26; p=0.24).

Interpretation ECT was not associated with risk of incidental dementia in patients with affective disorders after correcting for the potential effect of patient selection or competing mortality. The findings from this study support the continued use of ECT in patients with severe episodes of mood disorders, including those who are elderly.

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Introduction

Electroconvulsive therapy (ECT) is an effective treatment method for severe episodes of mood disorders,1 with major depression being the most important indication.^{2,3} Although ECT has beneficial acute effects such as reduction of psychotic and mood disorder symptoms, 1,3 memory loss is a common sideeffect that seems to be especially associated with bilateral lead placement and increasing number of treatments.^{1,4} Although most cognitive deficits resolve within weeks after treatment,5 any potential long-term adverse cognitive outcomes are less clear and subject to debate.1,3,4 Only a few studies have examined the frequency of dementia in patients after ECT. In one study⁶ of 81 Australian patients with major depression treated with ECT and followed up over 5 years, a greater number developed dementia compared with the general population (11 [14%; 95% CI 7-23]). In patients aged 75 years and older, the prevalence of dementia was three times higher than that in this age group in the general population (36% vs 11%).6 Another study from Sweden7 showed that 16 (34%; [95% CI 21-49]) of 47 patients with depression who underwent ECT were diagnosed with dementia about 10 years after ECT.7 However, both studies were hampered by small sample sizes and did not contain a reference group of patients with depression who did not receive ECT. By contrast, findings from a pilot study of 12 patients (mean age 59 years [SE 21.9]) with major depression suggested that ECT might reduce the risk of developing Alzheimer's disease by increasing the mobilisation of amyloid β_{14} in the cerebrospinal fluid. Thus, at present,

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Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospitals, Frederiksberg, Denmark (Prof M Osler DMSc. GT Christensen PhD); Department of Public Health, University of Copenhagen Copenhagen, Denmark (Prof M Osler, M P Rozina MD. GT Christensen, Prof P K Andersen DMSc); Danish Ageing Research Center, Department of Public Health, University of Southern Denmark, Denmark (Prof M Osler, GT Christensen); Center for Healthy Aging, University of Copenhagen, Copenhagen, Denmark (M P Rozing); and Psychiatric Centre Copenhagen Dept O, Rigshospitalet and Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark (Prof M B Jørgensen DMSc)

Correspondence to: Prof Merete Osler, Center for Clinical Research and Prevention, Bispebierg and Frederiksberg Hospitals, Frederiksberg 2000, Denmark

merete.osler@regionh.dk

Research in context

Evidence before this study

Electroconvulsive therapy (ECT) is an effective treatment for severe episodes of mood disorder, especially major depression. Although temporary memory loss is a common side-effect from this treatment, little is known about the long-term adverse cognitive outcomes. We searched PubMed for English-language articles published up to Sept 1, 2017, with the terms "electroconvulsive therapy", "ECT", "dementia", "depress*", and "risk" in various combinations. We retrieved 38 abstracts, and after screening them by abstract and reference lists of reviews on the safety of ECT, we identified two studies in which the frequency of dementia was assessed in patients treated with ECT. These studies included 81 and 47 patients, respectively, and did not contain a reference group of patients not treated with ECT. Thus, no adequately powered studies have been done that examine the risk of dementia following ECT in patients with severe mental illness.

Added value of this study

To our knowledge, this is the first study to show that ECT was associated with a decreased incidence of dementia in patients aged 70 years and older with affective disorders, which might be explained by factors related to patient selection and competing mortality. In younger patients, the incidence of dementia was low and the results were less conclusive.

Implications of all the available evidence

Potential adverse effects of ECT on cognitive function could fuel the fear of dementia in patients and clinicians, and for that reason, they might hesitate to choose ECT as a treatment. The present study shows that notwithstanding other possible adverse long-term cognitive effects, ECT is not associated with an increased risk of dementia. This finding supports the continued use of ECT in patients with severe episodes of mood disorders, including those who are elderly.

data for the long-term effects of ECT on patients' cognition and risk of dementia are conflicting.⁸

Against this background, the aim of our study was to examine the association between ECT and risk of subsequent dementia in a cohort of patients with a first-time hospital diagnosis of affective disorder.

Methods

Study design and participants

We did a cohort study of all citizens in Denmark aged 10 years and older with a first-time hospital contact for an affective disorder from Jan 1, 2005, through Dec 31, 2015. We identified inpatients and outpatients in the Danish National Patient Registry (DNPR)° with ICD-10 codes F30.0–F39.9. This register includes data on diagnosis and time of admission for all inpatient and outpatient hospital contacts in Denmark since 1995.° We classified patients by their main diagnosis at first admission (appendix).

A subsample of the population was also registered in the Danish Conscription Database with information from conscription board examinations at age 19 years on nearly all Danish men born between 1939 and 1959. In this cohort we identified men with a first-time hospital contact for an affective disorder from Jan 1, 2005, through Dec 31, 2015. The study was approved by the Danish Data Protection Agency.

Procedures

From the DNPR we retrieved information on all ECTs registered for patients with codes from SKS, a Danish health-care classification system (appendix)^{9,11} that reflected electrode placement and whether the treatment was involuntary or voluntary. Treatment with ECT (including information on electrode placement) was

defined at the time of first registration. The number of ECTs was counted from study entry until censoring, and dichotomised between ten or fewer sessions and more than ten sessions based on the median number of ECT sessions necessary for remission.¹¹

Outcomes

The outcome of interest was incidental dementia ascertained by physician diagnosis from the DNPR. We obtained diagnostic information on all first emergency-department contacts and inpatient or outpatient hospital contacts from Jan 1, 2005, through Oct 31, 2016, with ICD-10 codes F00·0–F03·9 and G30·0–G30·9. We also had data on previous dementia diagnoses registered in the DNPR or Danish Psychiatric Central Register since 1969 (coded with ICD-8: 290 diagnoses between 1969 and 1995). The validity of dementia diagnoses obtained from the DNPR has been assessed in two studies and they showed that 70% and 83% of dementia cases diagnosed by an external rater according to ICD-10 conformed to the diagnosis in the register 12.13 with the lowest validity in younger patients.

We supplemented our definition of dementia with data on individual patients' refill of at least one redeemed prescription of an acetylcholinesterase inhibitor identified by the Anatomic Therapeutical Chemical classification system codes (N06D) in the Danish National Prescription Registry. This register contains information on all prescribed and redeemed drugs sold at Danish pharmacies since 1995. Information on the incidence of dementia in the general Danish population was obtained from a report based on national register data. We also analysed the effect of electrode placement and the number of ECT sessions on the risk of developing dementia. If any negative effect of ECT on

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