Electroconvulsive Therapy for Major Depression in the Oldest Old

Effects of Medical Comorbidity on Post-Treatment Survival

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This is a longitudinal study of 65 patients who were 80 years old or older at the time they were hospitalized for depression. Thirty-seven were treated with ECT and 28 with medication. Survival after 1, 2, and 3 years in the ECT group was 73.0%, 54.1%, and 51.4%, respectively. Survival after 1, 2, and 3 years in the non-ECT group was 96.4%, 90.5%, and 75.0%, respectively. The relatively high mortality rate in the ECT group in this study suggests that patients over 80 who undergo ECT have more severe physical illness than those who can be treated successfully with medication. Medical comorbidity is a major determinant of long-term outcome of depression in the oldest old.

This study was designed to examine the long-term outcome of individuals with major depression who were over age 80 at the time of psychiatric inpatient hospitalization. After we reviewed the clinical and epidemiologic literature on depression in the elderly, it became clear that there is a lack of available information on the mortality and survival of this "old-old" group following hospitalization for major depression. Our primary objective was to add to the clinical knowledge of the outcome of ECT treatment in the very old and to help to enable predictions on the likelihood of recovery. We compared the survival rate of 80-year-old inpatients treated for major depression with ECT with patients who received non-ECT treatment.

A precondition for recovery from any illness is survival. When considering the prognosis of depression in patients over 80, one must keep in mind that 6.6% of the general population over age 80 will not reach the age of 81. By comparison, expectation of death in an average person between ages 50 and 51 is only 0.5%.[1]

Recovery is also related to the intrinsic mortality of the primary illness, in addition to the mortality of any coexisting illness. Major depression is a common disorder

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among the elderly and results in a significant amount of mortality if left untreated. Roth[2] found a mortality rate of 14.8% at 6-month follow-up in a group of 54 depressed patients, all of whom were over age 60. More recently, Avery and Winokur[3] compared the mortality of patients with depression, age 60 or older, who had been treated with ECT with those who had been treated with neither ECT nor antidepressants and found 3-year mortality rates of 5.1% and 21.1%, respectively.

The association between affective disorder and mortality in the general population has been a major focus of a 16-year investigation by Murphy et al.[4] A summary of outcome that combined mortality from any cause with psychiatric morbidity revealed that 75% ($n = 41$) of the individuals 60 years old or older who had depression, anxiety, and/or affective disorder at baseline had a poor outcome at follow-up. Overall, 82% of the sample with depression at baseline had a poor outcome 16 years later.

In an effort to measure mortality in a psychiatric population, Martin et al.[5] established the mortality status for 494 subjects during follow-up. A significant excess in mortality was observed among patients with diagnoses of antisocial personality disorder, alcoholism, schizophrenia, drug addiction, organic brain syndrome, homosexuality, and secondary affective disorder. Excess mortality was not observed among patients with primary affective disorder, using the distinction that secondary affective disorder was preceded or accompanied by a life-threatening, serious, or incapacitating medical illness. It is of interest that an excess of mortality was not found in any psychiatric category in the two oldest age groups, 65–74 years and 75–84 years.

Nevertheless, when considering the mortality of patients who have major depression and who are over the age of 80, one must take into account the statistically diminished expectation of survival because of the high rate of comorbid, age-associated medical illness. This factor alone contributes to the unique aspects of depressive disorders in this age group and has a likely effect on prognosis.

This nonexperimental study was part of a historical cohort study of hospitalized patients with mood disorder. Roughly 12% of admissions to our Psychiatric-Medical Inpatient Unit at Rhode Island Hospital are over age 80. This contrasts with the 5.2% of the general population who are over age 80. Rhode Island has the fourth highest percentage of residents over age 65 (14.7%), after Florida (17.8%), Pennsylvania (14.8%), and Iowa (14.8%).[1]

METHODS

We included in a chart review all patients hospitalized between 1974 and 1983 at the Rhode Island Hospital who were over the age of 80 when admitted and who had a discharge diagnosis of any of the following: major affective disorders (from DSM-II[6]), involutional melancholia (from DSM-II), affective psychosis (from ICD-8[7]), depressive disorder (from ICD-9[8]), major depression (from DSM-III[9]), or atypical depression (from DSM-III). Patient charts that had clear historical or clinical criteria for DSM-III-R[10] definition of major depression were included and labeled as the index admission.

A sample of 10 records, 5 with and 5 without criteria for major depression, was reviewed separately by two independent raters to establish the reliability of the method of subject selection; raters agreed on all 10 charts. Treatment modalities were then ascertained. Patients receiving ECT were initially evaluated separately ($n = 37$). This includes 9 patients who were intolerant of medications. The others received ECT because of severity of symptoms, treatment refractoriness, psychotic features, or a good past response to ECT.

To observe and quantify the survival of all patients over age 80 following inpatient treatment for major depression, we identified a comparison group of patients who

were also hospitalized for major depression but did not receive ECT (n = 28). This group consisted of 12 patients from Rhode Island Hospital and, as a way to increase the number in this reference group, 16 patients from Fuller Memorial Hospital, an 82-bed private psychiatric hospital in southern Massachusetts.

Hospitalizations for clear and/or established organic brain syndromes (DSM-II), depressive neurosis (DSM-II), dysthymia (DSM-III), or organic affective disorder (DSM-III) were excluded in both groups. Length of stay (in days) in hospital was determined from the charts as was the length of follow-up, which was calculated from the date of index admission.

Information pertaining to next of kin and/or relatives, subsequent admissions, and residence status was collected from the chart. Letters were addressed and sent to the patient with reference to our intended study and purpose. Interview was via telephone survey (by D.K.) using the following hierarchy of interviewees: patient, spouse, child, sibling, physician, friend, other professional caretaker. If a person on the list was unavailable, deceased, or unable to give complete information, the next person on the hierarchy was invited to contribute information. Interviews were stopped when the standardized semistructured interview was complete, when the list of interviewees was exhausted, or when there was a lack of cooperation. Attempts were made to ascertain the following information: pre- and posthospitalization residence status, recurrence of depressive features, the need for rehospitalization (psychiatric and/or medical), medications (inhospital, posthospital, current), condition on discharge, additional courses of ECT, and a subjective report on present functional status. Recurrence rates were determined by subjective report during the follow-up interview. Patients or interviewees were asked if the depression recurred.

If a patient was deceased, the date and cause of death was determined. In six of the deceased, the date and cause of death were obtained through the Rhode Island State Department of Vital Statistics. There were three patients in the non-ECT group on whom follow-up information was not available.

Survival experience for all patients was then compiled for analysis. For this study, survival was measured from the index admission date to either the time of telephone interview or to the time of death. Estimation of the survival curve was calculated by analysis of the survival data as described by Kaplan and Meier.[11] The essential concept of this "actuarial" survival curve involves the recording of survival times for n individuals and r of these times exceed a specified time, t, where r refers to the number of surviving individuals at risk. The natural estimate of the probability of surviving more than t units would be r/n. The Kaplan-Meier methodology produces a nonparametric estimate of survival when all the survival times are not exactly known. For instance, if death has not occurred by t, then survival time must exceed t and the resulting survival curve reflects this probability.

Comparison of the Kaplan-Meier curves for both treatment groups was calculated by the log-rank or Mantel-Haenszel test,[12,13] which is designed to detect differences between survival curves from two groups. This test is especially useful when the survival rate in one group is consistently higher than the corresponding survival of another group and the ratio is constant over time. The log-rank test was chosen as the test for survival comparison because it gives equal importance to all deaths within comparison groups, as opposed to the generalized Wilcoxon test, which attaches greater importance to earlier rather than later deaths. The goal of this study was to view longitudinal survival with different points of entry.

RESULTS

Table 1 provides a summary of the demographic data for the two comparison groups.

TABLE 1. Characte given EC for depre

Total (N = 65)
Male (n = 17)
Female (n = 48)
Mean age, years, at index admission
Male
Female
Length of follow-up, n median/interquartile

We found a total 80 years old or ol pitalized for depre were treated with primarily with mec non-ECT group cc pressants (n = 20; 15), trazodone (n = chloral hydrate (n = = 2), maprotiline (n = = 1), and nomifens

Table 2 summa comes. At the end were 31 individual male to male ratic endpoint (2.9:1) wa and non-ECT (2.8 sponds to the ba cause of death in cluded cancer (n = (i.e., pneumonia, s aspiration, or urose rest or congestive h intestinal obstructic (n = 1), cerebral va suicide (n = 1), and

The mean nun 2.9. Two patients patient withdrew c developed CHF and be continued. The interval between E months with an int months. The numbe

TABLE 1. Characteristics of patients over 80 given ECT and non-ECT treatment for depression

	ECT	Non-ECT
Total (N = 65)	37 (56.9%)	28 (43.1%)
Male (n = 17)	9	8 (26.1%)
Female (n = 48)	28	20 (73.9%)
Mean age, years,		
at index admission	83.0	82.5
Male	83.0	82.1
Female	83.0	82.6
Length of follow-up, months		
median/interquartile range	34/43	30/35

We found a total of 65 patients who were 80 years old or older when they were hospitalized for depressive illness. Thirty-seven were treated with ECT and 28 were treated primarily with medication. Treatment of the non-ECT group comprised tricyclic antidepressants (n = 20), benzodiazepines (n = 15), trazodone (n = 6), neuroleptics (n = 5), chloral hydrate (n = 2), lithium carbonate (n = 2), maprotiline (n = 1), carbamazepine (n = 1), and nomifensine (n = 1).

Table 2 summarizes treatments and outcomes. At the endpoint of the study there were 31 individuals (47.7%) alive. The female to male ratio of those living at the endpoint (2.9:1) was similar in the ECT (3:1) and non-ECT (2.8:1) groups and corresponds to the baseline rate (2.8:1). The cause of death in the 34 individuals included cancer (n = 8), "failure to thrive," (i.e., pneumonia, septicemia, dehydration, aspiration, or urosepsis; n = 8), cardiac arrest or congestive heart failure (CHF; n = 7), intestinal obstruction (n = 2), renal failure (n = 1), cerebral vascular accident (n = 1), suicide (n = 1), and unknown (n = 6).

The mean number of ECTs was 7.9 ± 2.9. Two patients had only 2 ECTs: one patient withdrew consent, and the other developed CHF and died before ECT could be continued. The median value for the interval between ECT and death was 20 months with an interquartile range of 45 months. The number of ECT treatments for any one patient was not significantly correlated with the likelihood of recurrence.

TABLE 2. Treatment and outcome of patients over 80 given ECT and non-ECT treatment for depression

	ECT	Non-ECT
Mean length of stay, days		
Median/interquartile range	32/20	19/14
At Rhode Island Hospital	32/20	30/15
At Fuller Mem. Hospital	na	18/9
Living at 1 year, %	73.0	96.4
Mortality, %		
At 1 year	27.0	3.6
At 3 years	48.6	33.3
Number living at endpoint		
of study (n = 31)	8	23
Male (25.8%)	2	6
Female (74.2%)	6	17
Mean age, living, years	87.5	85.0
Male	84.5	85.9
Female	88.5	84.6
Recurrence		
Yes = 27 (41.5%)	20 (54.1%)	7 (25.0%)
No = 28 (43.1%)	8 (21.6%)	20 (71.4%)
Unknown = 10 (15.4%)	9 (24.3%)	1 (3.6%)
Rehospitalization		
Yes	9	3
No	11	4
Unknown	8	1
Additional ECT		
Yes	6	na
No	23	na
Unknown	8	na
Residence after hospitalization		
Nursing home	18	8
Own home	17	15
Unknown	1	5

Note: For a description of outcome measures, see text. Patients who had a recurrence are incorporated in rehospitalization category.

We found an overall recurrence rate of 41.5%, with 54.1% in the ECT group and 25.0% in the non-ECT group. The mean age at index admission of those who had recurrence of depression was 83.0 years, compared with a mean age of 82.8 at admission for those who did not have recurrence. Lasting recovery was achieved in 43% of our patient population (22% in the ECT and 71%

TABLE 3. Survival rates of patients over 80 given ECT and non-ECT treatment for depression

	Survival Rate, %		
	1 year	2 years	3 years
ECT	73.0	54.1	51.4
Non-ECT	96.4	90.5	75.0

in the non-ECT group), which is considerably greater than the study of Baldwin and Jolley[14] (21.9%) and the two studies by Post[15,16] (30.8% and 26.1%, respectively). If recurrence was measured by the rehospitalization rate, then the difference between the two groups would be less significant (41% for the ECT group and 15% for the non-ECT group). "Recurrence yet not hospitalized" could be considered to be a "soft" relapse, the significance of which should be questioned. The rehospitalization rate from this study coincided with the rehospitalization rate for geriatric depression in the study by Colenda et al.[17]

The estimated survival curves for the ECT group, the non-ECT group, and the normal population (from U.S. Census data) are shown in Figure 1. As can be seen, the "curve" is derived from horizontal sections, which represent the intervals of time that deaths were not observed, and vertical steps, which represent the number of deaths recorded at t months. The analysis of survival differences for the two treatment populations revealed constant differences across time. The significance level using the Mantel-Haenszel calculation is $0.005 > P(\chi^2 > 14.20) > 0.001$; this supports the conclusion that there are true differences in the survival of the two groups.

Table 3 gives the 1-, 2-, and 3-year survival rates after discharge from hospital. At 1 year we established a 73.0% survival rate for the ECT group and a 96.4% survival rate for the non-ECT group. At 3 years, the survival rate of the ECT group was 51.4% compared with 75.0% for the non-ECT group. These survival rates are lower than those of the group age 60 years or older treated with ECT ($n = 39$) in the study of Avery and Winokur,[3] who found a 97.4% 1-year survival rate and a 94.9% 3-year survival rate.

It can be seen from Table 3 that the survival of the ECT group had a higher rate of decline between the first and second year than between the second and third year. This suggests that mortality from combined depression and unstable medical illness is highest in the first 2 years following treatment, after which survival parallels the aged-matched general population. ECT did not appear to interfere with the normal propensity for survival in our elderly sample, and this corresponds to the findings of Gaspar and Samarasinghe[18] and the conclusion of Benbow[19] that ECT is safe in the medically compromised elderly.

DISCUSSION

The findings of this study suggest that patients over 80 years old who receive ECT for major depression are at increased risk for death over the 2 years following treatment. The mortality rates for these patients exceed the rates for patients of comparable age treated in a hospital without ECT, and both exceed published rates for mortality following depression in younger patients.[3,20] The variance was not, however, due to the use of ECT and had more to do with patient characteristics.

Although it was not the ultimate intent of this study to measure treatment efficacy, attention was paid to the possibility for selection and treatment-monitoring biases. The selection of subjects was solely by age, illness, and hospitalization status and, while there were a few subjects who could not be reached during follow-up, our ability to recruit participants was good to excellent. Accuracy and reliability of historical information was likely subject to both interviewer bias and recall bias, an inherent limitation of this and most other historical cohort studies. Underreporting or over-

Recovery - Survival RATE

FIGURE 1. Kaplan

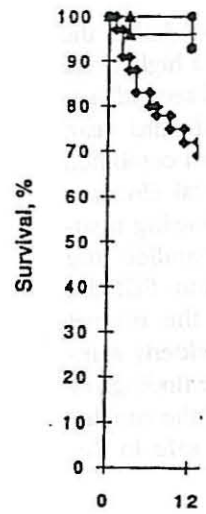

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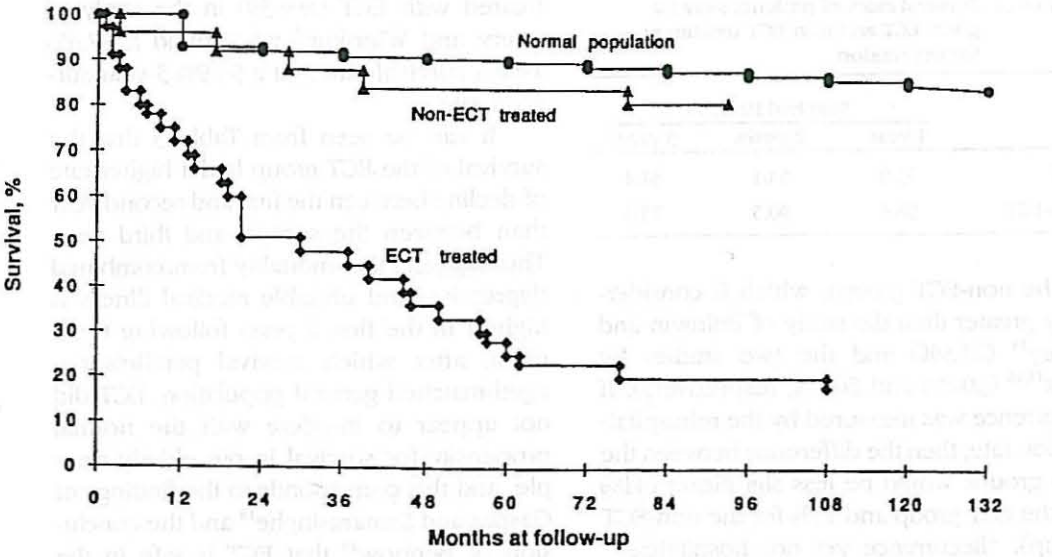
FIGURE 1. Kaplan-Meier actuarial survival curve



reporting of clinical information by the respondent is also a source of potential bias in this type of study design. The validity of the comparison in this study can be strengthened by the fact that none of the subjects refused to participate and the courses of illness for both groups were similarly monitored, as was the follow-up procedure. In addition, all subjects were hospitalized and treated during roughly the same time period, thereby keeping treatment practices standard.

The pretreatment clinical characteristics of both groups were more important than any of the other measured variables. The most obvious covariates were the presence of medical illness, the need for close ancillary medical attention, and severity of depression. The ECT group was both medically debilitated and mentally more ill, which was supported by the increased length of hospital stay, the higher recurrence rate, and the increased need for extended care in a nursing home. The patient populations in both hospitals differed, reflecting the clinical function of each hospital. The Medical-Psychiatry Unit at Rhode Island Hospital focuses on patients with comorbidity, whereas Fuller Memorial Hospital has a lower threshold for medical/psychiatric comorbidity.

For this reason the mortality and survival of the non-ECT group cannot be compared with the ECT group with statistical significance, yet these rates should be compared as a measure of the effect of physical illness on outcome. One way to strengthen this and other similar studies would be to record the number of medical diagnoses or the number of total medications and then make adjustments in the analysis. Nevertheless, our finding that those depressed patients with diminished survival were more likely to be suffering from chronic physical illness coincides with the study of Murphy,[21] who found that of 124 elderly depressed patients, 49% of the "poor outcome" group had major chronic physical health problems compared with 29% in the "good outcome" group.

The group of elderly patients who received ECT could be considered to be at a relatively higher risk because of their advanced age and physical illness, yet we did not find an increase of ECT-related mortality or morbidity in these very old individuals.

This is in contrast to Alexopoulos et al.,[22] who found medical problems arising during ECT to be significantly more common in those over age 65. We conclude that ECT is effective and useful in patients over age 80 with the same margin of safety as in younger populations, as long as attention is given to the optimal management of comorbid medical illness. People over age 80 can be treated successfully and safely with ECT.

In addition, and contrary to Babigian and Guttmacher,[20] who found that women aged 75 years treated with ECT had substantially decreased mortality compared with age-matched non-ECT-treated groups, we found increased mortality in the ECT-treated group. The increased mortality in our study can be viewed as a reflection of the prevalence of severe physical illness in the group of patients who received ECT. The small number of patients in this study did not allow for calculation and comparison of cause-specific deaths in proportion to the standard, nondepressed population. All deaths, rather than cause-specific deaths, were included for estimation of relative survival. It would be important to establish whether treatment of depression with ECT has a positive effect on the mortality from and comorbidity of medical diseases.

The number of patients suffering from "first episode of depression" at the index admission vs. a history of "recurrent depressive episodes" was not ascertained, and this may identify patients with more refractory depressive disorders. It is also unclear how many of the index admissions and readmissions were preceded by apparent or occult medical illness. In some cases, the physical illness was manifest, but in others, an underlying problem, such as an occult cancer, may have increased the severity and refractoriness of depression before the medical illness was apparent.

In this study the survival characteristics varied with the type of treatment, which is not to say that the treatment directly affected survival. The variance is a function of the clinical heterogeneity of our patient population and it appeared that the non-ECT group had the same survival rates as the general population. The psychiatric follow-up data, while limited, show that those patients who did not die had a reasonable chance of remaining in the community and avoiding rehospitalization for recurrent depression.

It became clear during the initial data collection of the non-ECT group that the survival characteristics of both groups could not be reliably compared because the ECT group was, in general, a sicker group. The high mortality rate in the ECT group suggests that patients over 80 who are referred for ECT have more physical illness and depressive symptomatology caused by physical distress than those who can be successfully treated with medication. These patients deserve particularly close follow-up because they are at a higher risk for life-threatening physical illness. In addition, further ECT outcome studies in this age group must give meticulous attention to medical comorbidity as a prognostic factor.

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