

RDC Alcoholism in Patients With Major Affective Syndromes: Two-Year Course

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The authors examined the 2-year course of alcoholism as defined by Research Diagnostic Criteria (RDC) in 127 newly admitted patients with major affective syndromes and concurrent alcoholism at intake. The cumulative probability of remission (at least 6 months free of alcohol problems) in these patients was 0.67. Many of the remissions began within a few weeks of intake; the remaining were distributed over the follow-up period. Of the patients without remissions, 17% died, half by suicide. Diagnoses of schizoaffective disorder, indicators of alcohol dependence, and previous chronicity of alcohol problems predicted poor outcome of alcoholism, but none of these variables predicted subsequent relapse.

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We have shown previously that many patients with affective syndromes abuse alcohol during episodes which bring them into treatment (1). Much literature exists on the course of alcoholism in patients treated in alcohol-identified settings, and epidemiologists also have studied persistence of alcohol problems in the community (2). However, the prospective study of concurrent alcoholism in psychiatric patients presenting primarily for treatment of other mental disorders appears to be relatively unresearched. In this pa-

per, we describe the patterns and predictors of remission and relapse of alcoholism diagnosed according to Research Diagnostic Criteria (RDC) (3) over 2 years of follow-up in patients concurrently treated for major affective syndromes. Specifically, we examine 1) the time to remission of alcoholism, 2) predictors of remission, 3) time to relapse in those who experienced a remission, and 4) predictors of relapse within the period at risk.

METHOD

The patients were a subset of the 955 participants in the NIMH Collaborative Study on the Psychobiology of Depression (Clinical Studies Section). Details of this study are described elsewhere (3–5). Briefly, subjects meeting RDC for major affective syndromes assessed with the Schedule for Affective Disorders and Schizophrenia (SADS) (4) were recruited from five medical school treatment settings. Of the initial sample, 135 patients received additional RDC diagnoses of probable or definite current alcoholism; 127 (94.1%) of these patients participated in the follow-up study.

All 127 patients were Caucasian, 51 (40.2%) were women, 39 (30.7%) were married, and 30 (23.6%) had never been married. Eight-six (67.7%) were under 40 years of age, and 96 (75.6%) had household incomes under \$22,000. Thirty-four (26.8%) of the patients were from Iowa City, 30 (23.6%) were from Boston, 41 (32.3%) were from St. Louis, and 22 (17.3%) were from New York or Chicago. Only 15 (11.8%) were outpatients. Six (4.7%) of the patients had schizoaffective disorder, manic or depressed type; 17 (13.4%) had bipolar I disorder; 10 (7.9%) had bipolar II disorder; and 94 (74.0%) had major depressive disorder.

The RDC intentionally provide a low-threshold, inclusive definition of “alcoholism.” Therefore, subjects

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can meet RDC for this disorder with milder drinking problems than would ordinarily be seen in alcoholism treatment settings. In this sample, some patients had only the minimum number of symptoms necessary to receive an RDC diagnosis of probable alcoholism and therefore experienced very low levels of alcohol difficulties. Others presented with a picture of considerable clinical severity. Out of a total of 18 possible RDC alcohol symptoms, the mean \pm SD number shown by the patients in this sample was 7.04 ± 3.77 . For comparative purposes, we note that the mean number of such symptoms in a random sample of 123 alcohol rehabilitation patients interviewed at about the same time was 9.88 ± 3.16 (6). For the purposes of this study, using the RDC alcohol diagnosis as an inclusion criterion allowed us the advantage of examining aspects of alcohol-related severity over a broad range.

Subjects were evaluated with the SADS and RDC as soon as possible after either admission to the hospital or their first outpatient appointment. These evaluations included information obtained from clinical staff, significant others, and previous medical records. All patients gave informed consent after the study had been explained.

Follow-up information for this study was obtained every 6 months by using the Longitudinal Interval Follow-Up Evaluation (5), which provides a format for separately charting the severity of multiple specific mental disorders (including RDC alcoholism) on a weekly basis. Clinical interviewers administering the Longitudinal Interval Follow-Up Evaluation probed for major changes in the patients' conditions during the preceding 6 months. When changes occurred, interviewers probed for the week in the study when the change occurred, exploring the relationship of these changes to holidays and other events if necessary.

In the Longitudinal Interval Follow-Up Evaluation, alcoholism was rated on a 3-point scale. A score of 1 indicated that the patient met criteria for a definite diagnosis, a score of 2 indicated some evidence of alcohol problems but not enough to meet full criteria for a diagnosis, and a score of 3 indicated no evidence of any RDC symptoms of alcoholism. Abstinence from alcohol was not required for the score of 3. However, raters explored very carefully for any RDC alcoholism symptoms when interviewing current drinkers with previous alcohol diagnoses.

For the analyses reported here, we defined "remission" from RDC alcoholism as 26 weeks or more with no evidence of any RDC alcohol symptoms. We required at least 26 weeks in order to study a change with some degree of stability in a condition that is often episodic. Relapse was defined as any occurrence of RDC alcohol symptoms following 26 weeks of remission as defined. The onset date of remission was week 1 of the 26 or more weeks required. The starting date of a relapse was the first week in which any alcohol symptoms occurred following 26 weeks of remission.

The potential predictors of 2-year course, evaluated

at intake, can be grouped as demographic, clinical-diagnostic, and alcohol specific. Since community surveys show that alcohol problems of young adults and women are more likely to remit than those of older individuals and men (2, 7, 8), we predicted that older subjects and male subjects would experience poorer outcome. We included living situation (alone versus with others) among the demographic variables on the grounds that lack of exposure to the social disapproval of others in the home might pose a risk factor for patients living alone. Literature on the effect of income has been mixed (9); we included income for descriptive purposes.

The clinical-diagnostic predictors included subtypes of affective disorder, cycling between poles during the index episode of affective disorder, a global measure of severity, and a diagnosis of antisocial personality disorder. Reich et al. (10) showed that heavy drinking was associated with manic phases of bipolar illness, so we predicted that patients with bipolar disorders would have worse outcomes. We did not have a specific prediction about schizoaffective disorder. Cycling between affective poles during the intake episode predicted very poor outcome of affective disorders (11) and was therefore expected to predict poor outcome of the alcoholism as well. We expected that poorer functioning or severity of illness as measured by the Global Assessment Scale (12) would predict poorer outcome of alcohol problems. Rounsaville et al. (13) showed that broadly defined antisocial personality disorder is prognostic of poor outcome for alcoholism, so patients with additional diagnoses of antisocial personality disorder were expected to experience poorer outcome of their alcoholism.

We included three alcohol-specific predictors. One concerned past chronicity. This often predicts future chronicity, so we included a variable representing brief (less than 6 months) or chronic duration of RDC alcoholism before entry into the study.

We derived the other two alcohol-specific predictors from concepts related to the Edwards-Gross alcohol dependence syndrome (14). This syndrome includes such symptoms as tolerance, withdrawal, drinking to relieve or avoid withdrawal, drinking increasingly unaffected by ordinary social conventions regarding appropriate drinking behavior, and the feeling of compulsion or impaired control (a key feature). The alcohol dependence syndrome was proposed as a continuous dimension of alcohol problems distinct from drinking-related social or occupational impairment (14). *DSM-III-R* and *ICD-10* draw more heavily on this concept of alcohol dependence than did earlier diagnostic systems (*DSM-III*, 3, 15). Although alcohol-related social and/or occupational problems have been shown to be somewhat transient in the general U.S. population (16), the alcohol dependence syndrome was conceptualized as prognostic of continued difficulties with drinking (17). Rounsaville et al. (13) showed that the severity of the alcohol dependence syndrome predicted poor outcome in treated alcohol-

ics. Therefore, we wished to distinguish indicators of the alcohol dependence syndrome from social-occupational problems and evaluate each as predictors of outcome.

Seven RDC items cover aspects of the alcohol dependence syndrome (feeling one can't stop, morning drinking, repeated benders, shakes, delirium tremens, hallucinations after drinking, and withdrawal seizures). We constructed a 7-item summation scale to measure the severity of the alcohol dependence syndrome with these dichotomous items. The scale had acceptably good internal consistency ($\alpha=0.70$ as determined with the KR-20 formulation of alpha, the standard formula for internal consistency with dichotomous items [18]). Items covering alcohol-related social-occupational problems from the SADS were treated similarly (others objecting, trouble with family or friends, divorce, job problems, losing a job, repeated violent behavior, driving problems, trouble with police) and also formed an acceptably reliable scale ($\alpha=0.68$).

Some patients died or were lost to follow-up without remission, and others had not remitted at all by the end of the 2-year follow-up period. Therefore, we used survival analyses. We obtained product-limit estimates of the probability of recovery for each week of the follow-up period. We found that site (potentially a multicategory control variable) was not significantly associated with time to recovery using Gehan's generalized Wilcoxon tests (19), so we did not control for this in further analyses. We tested the univariate association of the predictor variables with time to recovery using Kalbfleisch and Prentice's extension of generalized Wilcoxon tests (20). Among patients with remissions, we used the same procedures for testing time to relapse. The Cox proportional hazards model to simultaneously examine the effects of multiple predictors of time to an event assumes that hazard ratios between groups are consistent over time. Plots of $\log(-\log)$ survival estimates by subgroup showed that this assumption was violated for several predictor variables. Therefore, we used simultaneous logistic regression to test whether the predictor variables conjointly gave approximately the same results as the univariate tests, regressing the predictor variables on 1) remission by 2 years (yes or no) and 2) relapse among those with remissions.

RESULTS

We followed 107 (84.3%) of the patients for the entire 2-year period. Eight patients were followed for a shorter period of time (range=2–91 weeks) because they died, including five who were followed for less than 6 months. The remaining 12 were either lost to follow-up or refused further participation before the end of the study period (range=26–78 weeks).

Over the 2 years of follow-up for this sample, the cumulative probability of remission from RDC alco-

FIGURE 1. Cumulative Proportion of Patients With Concurrent Affective Disorders Who Recovered From Index Episode of RDC Alcoholism (N=127)

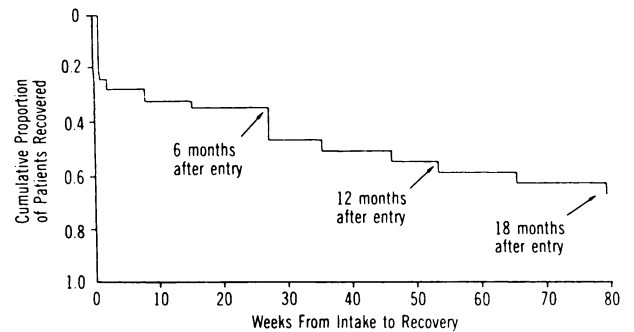


TABLE 1. Predictors of Time to Remission of RDC Alcoholism in 127 Patients With Concurrent Affective Disorders^a

| Predictor | χ^2 (df=1) |
|---------------------------------|--------------------|
| Age | 1.02 |
| Sex | 0.55 |
| Living alone | 0.00 |
| Income | 0.95 |
| Diagnosis | |
| Schizoaffective disorder | 4.08 ^b |
| Bipolar I | 0.21 |
| Bipolar II | 5.48 ^c |
| Antisocial personality | 0.21 |
| Global Assessment Scale score | 0.03 |
| Alcoholism longer than 6 months | 10.04 ^d |
| Alcohol dependence indicators | 6.41 ^c |
| Social-occupational problems | 0.63 |

^aRemission was defined as 26 weeks or more with no evidence of any RDC alcoholism symptoms. Predictors were determined with univariate survival analysis.

^bSignificantly associated with poorer outcome ($p<0.05$).

^cSignificantly associated with better outcome ($p<0.05$).

^dSignificantly associated with poorer outcome ($p<0.01$).

^eMore indicators significantly associated with poorer outcome ($p<0.05$).

holism for at least 6 months was 0.67. Of the 79 patients who remitted, the cumulative probability of relapse by the 2-year point was 0.29. None of the patients with remissions (either sustained or not) had died by the end of the 2 years. Of the 48 patients without remissions, eight (16.7%) died; four by suicide. Two of the others died while heavily intoxicated (one of exposure, one from aspirating vomit). One was fatally shot in a bar during a holdup, and the last died of cancer.

Figure 1 shows the product-limit estimates of the probability of remission, by week, during the 2 years. As shown, many remissions occurred during the first several weeks. By 12 weeks, the cumulative probability of remission was 0.34. However, patients continued to remit throughout the time in which subjects could cease experiencing drinking problems and remain in this state for 26 weeks (week 78). At 6 months, the

TABLE 2. Cumulative Probability of Remission of RDC Alcoholism in Subgroups of Patients With Concurrent Affective Disorders^a

| Subgroup | Cumulative Probability of Remission | | | |
|--|-------------------------------------|---------|---------|----------|
| | Week 12 | Week 26 | Week 52 | Week 104 |
| Schizoaffective disorder (N=6) | 0.17 | 0.17 | 0.17 | 0.17 |
| Bipolar II disorder (N=10) | 0.70 | 0.70 | 0.85 | 0.85 |
| Alcohol problems for less than 6 months (N=24) | 0.63 | 0.71 | 0.76 | 0.81 |
| Three or more alcohol dependence indicators (N=43) | 0.23 | 0.26 | 0.39 | 0.50 |
| Total (N=127) | 0.34 | 0.37 | 0.52 | 0.67 |

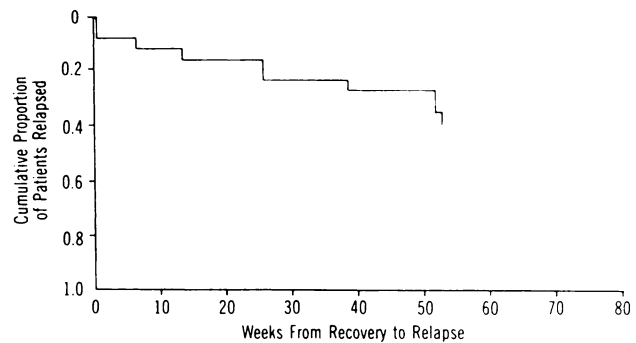
^aProbability of remission was determined by using product-limit estimates. Only subgroups that showed statistically significant differences are listed.

cumulative probability of remission was 0.37; at 1 year, 0.52; and at 2 years, 0.67.

Table 1 shows the results of the tests for the association of the predictor variables with time to remission from alcoholism. Neither age, gender, living alone, nor household income had a significant relationship to time to remission. In contrast, even with only six patients with schizoaffective disorder and consequently little statistical power, schizoaffective disorder was significantly related to longer time to remission. As shown in table 2, the cumulative probability of remission for the patients with schizoaffective disorder by the end of follow-up was only 0.17. RDC Bipolar II (also rare, N=10) was also significantly related to remission, but in the opposite direction; the cumulative probability of remission for subjects with this subtype was 0.85 by the 2-year point. No other clinical-diagnostic variable was significantly associated with time to relapse. Table 2 shows the cumulative probabilities of remission for the subgroups that showed statistically significant differences.

In this sample, 24 (18.9%) of the subjects experienced only brief alcohol problems (6 months or less) before entry into the study. As shown in table 2, we found that brief duration was associated with earlier remission. We also found that higher scores on the dependence scale were associated with poorer outcome. However, the social-occupational dimension of alcohol-related problems was not significantly associated with time to remission, even though subjects had scores throughout the entire range of severity on this scale, from none of these problems (seven patients, or 5.5%) to seven or eight of them (10 patients, or 7.9%)

As already noted, logistic regression was used as a partial check on whether the results of the univariate tests would hold up in a multivariate analysis. Regressing remission (yes or no) on the independent variables listed in table 1 produced results similar to those obtained with the individual tests, although some statistically significant predictors in the Wilcoxon tests just missed statistical significance in the logistic regression (schizoaffective disorder, $\chi^2=5.66$, n.s.; alcohol dependence indicators, $\chi^2=5.24$, $p<0.05$; bipolar II disorder,

FIGURE 2. Cumulative Proportion of Patients With Concurrent Affective Disorders Who Recovered From Index Episode of RDC Alcoholism But Then Relapsed (N=79)

der, $\chi^2=3.17$, n.s.; alcoholism longer than 6 months, $\chi^2=2.81$, $p<0.10$) (all values for $df=1$). Since we did not find major decreases in significance levels in the multivariate test, we concluded that our univariate survival analyses of remission were not spurious due to confounding or redundancy of variables.

Since alcoholism treatment was not randomly assigned to the patients in this study, we could not assess the influence that treatment had on outcome, although there was a slight (nonsignificant) tendency for patients with worse outcome to have had treatment specifically for alcohol problems during the follow-up period. Six (7.6%) of the 79 patients with a remission were treated in inpatient detoxification, nine (11.4%) received treatment in alcohol rehabilitation, 15 (19.0%) attended Alcoholics Anonymous (AA) during the 2 years, and 15 (19.0%) took disulfiram. Of the 48 patients without a remission, 11 (22.9%) had inpatient detoxification, seven (14.6%) were treated in alcohol rehabilitation, eight (16.7%) attended AA, and 10 (20.8%) took disulfiram.

We next considered relapse. Figure 2 presents the product-limit estimates of the probability, by week, of relapse after 26 weeks of remission. The times at risk for relapse were quite variable because subjects who began remissions later had less time at risk for subsequent relapse. As shown, relapse was more evenly spread over time than initial remission. No variable tested as a predictor of remission was significantly associated with relapse.

DISCUSSION

These data illustrate that the outcome of problem drinking in patients with major affective syndromes is quite variable. A number of the patients in this sample ceased experiencing alcohol problems almost immediately after entry into the study. Others took longer to remit. About two-thirds of those whose alcohol problems remitted maintained this status, while others relapsed. A high proportion of subjects who did not remit died, consistent with the literature indicating

increased mortality among those with alcohol problems (21–23).

Previously (1), we found that subtype of affective syndrome did not predict concurrent alcohol problems. However, certain subtypes do seem to predict outcome once alcohol problems have commenced. Patients with schizoaffective disorder were unlikely to remit from drinking problems, and the follow-up case narratives of these patients indicated that they generally had a very hard time and were difficult to treat. Bipolar I disorder was not associated with time to remission, perhaps because manic episodes during the follow-up were treated quickly enough to prevent problems from mania-related drinking. We are unsure how to explain the finding that patients with bipolar II disorder had a significantly shorter time to remission.

We did not find the predicted relationship of antisocial personality disorder with poor outcome. Woody et al. (24) found that opiate addicts with major depression and antisocial personality disorder improved after treatment, but opiate addicts with antisocial personality disorder and no depressive disorder showed little improvement. Rounsaville et al. (13) did not differentiate their antisocial alcoholic subjects into those with and those without major depression. Perhaps depression in alcoholic antisocial individuals (such as those included in this report) indicates a difference in personality structure; such individuals might have a greater capacity to engage in treatment and improve than do individuals with antisocial personality disorder who do not become depressed.

Defining “remission” or “recovery” from alcoholism is difficult and somewhat controversial. Some may find our definition too rigid, while others may object that we did not require complete abstinence from alcohol. We would have preferred to analyze outcome on many dimensions of alcohol problems, but such information was not available. Given the scarcity of information on our topic, the analyses seemed warranted with the data at hand. Future research on the outcome of alcohol problems in patients with mental disorders would be improved by separate measurement and analyses of many dimensions of alcohol dependence and related difficulties.

An additional measurement issue is the validity of self-report information on alcohol consumption and problems. Information was corroborated at times from other informants, but not routinely. However, family reports often do not reveal alcohol problems that subjects themselves are willing to discuss with research interviewers (25). Some of our subjects probably minimized their difficulties with drinking, but they were the only ones who could report on the more subjective aspects of their drinking experiences.

Also, patients were probably not completely accurate in the dating of remission and relapse. Some patients may have remembered exactly when their remissions began (for instance, AA members who could date anniversaries of abstinence), but this was not such a clearly demarcated event for others. Nevertheless, us-

ing subjects' estimates of the timing of a remission probably provides more information than simply noting remission as a yes-or-no phenomenon at some point in time. Even if subjects miscalculated by a month or two, the fact that the information was reviewed with subjects every 6 months served to locate approximately when the remission took place.

The criteria for the Edwards-Gross alcohol dependence syndrome (14), introduced in 1976, now form much of the basis for the alcohol dependence criteria of both *DSM-III-R* and *ICD-10*. Although research is needed on the psychometric properties of these criteria, the fact that dependence indicators predicted outcome while social problems did not argues for the differentiation of at least these two dimensions of alcohol use disorders. A possible implication of the finding is that multiple indicators of the alcohol dependence syndrome can be taken as evidence of a drinking problem for which the goal of abstinence may be an especially important part of the treatment.

We were unable to identify significant predictors of relapse among the patients whose alcohol problems remitted. However, the time at risk for a relapse was much shorter than the time in which patients could show a remission. Data will soon be available on these patients for an additional 3 years, allowing more complete analysis of relapse over an extended period of time.

Our results were obtained for patients with particular types of mental disorders, and generalizability to patients with other disorders is not known. Given the high rates of comorbidity of alcoholism and various mental disorders, this is an area in which more research is needed. As information becomes increasingly available on these issues, clinicians may be more likely to address such problems in their patients, improving the chances of a good treatment outcome for all concurrent disorders.

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