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Relapse after abrupt discontinuation of maintenance electroconvulsive therapy during the COVID-19 pandemic

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Abstract

Objective: Maintenance electroconvulsive therapy (M-ECT) is considered an effective relapse prevention strategy in severe mood and psychotic disorders. How long M-ECT should be continued, and what the outcome is after its discontinuation has not been adequately studied. In our tertiary psychiatric hospital, M-ECT treatments were suspended at the start of the COVID-19 pandemic. We aimed to determine the 6-month relapse rate and time to relapse after abrupt discontinuation of M-ECT and to assess the impact of patient and treatment characteristics on the risk of relapse.

Methods: Eighty-one patients whose M-ECT was discontinued abruptly were followed up prospectively for 6 months, or until relapse (i.e., hospital admission, restart of ECT, change of pharmacotherapy, or suicide (attempt)). We used multivariable Cox proportional hazards models to assess the impact of patient and treatment characteristics on the risk of relapse.

Results: Thirty-six patients (44.44%) relapsed within 6 months following abrupt discontinuation of M-ECT. A greater number of previous acute ECT courses, a diagnosis of psychotic disorder (compared with major depressive disorder or bipolar disorder), and a shorter interval between M-ECT treatments at the time of discontinuation were significantly associated with increased risk of relapse.

Conclusion: Almost half of the patients relapsed, similar to the relapse rate after a successful acute course of ECT. Patients with a shorter interval between M-ECT treatments at the time of discontinuation seem to be at increased risk, as well as patients with a diagnosis of psychotic disorder, compared to patients with mood disorders.

KEYWORDS

COVID-19, discontinuation, maintenance electroconvulsive therapy, relapse

1 | INTRODUCTION

Electroconvulsive therapy (ECT) is an effective treatment for patients with severe mood and psychotic disorders.[1] As with pharmacotherapy, however, relapse rates following a successful acute treatment are high and constitute a major clinical problem. Despite continuation treatment using medication or ECT, half of the patients with unipolar or bipolar depression experience relapse within a year following a successful acute course of ECT, with the first 6-month period encompassing the highest risk.[2] Likewise, in patients with schizophrenia, 1-year relapse rates range from 40% to 60%.[3] Although relapse rates remain high, continuation and maintenance treatment using ECT is considered an effective strategy to prevent relapse following a successful acute course of ECT.[3-5] It is generally reserved for patients who have had multiple, severe episodes and have failed to remain well on pharmacotherapy.[1] Evidence suggests that maintenance treatment with ECT, even when administered for several years, does not cause cumulative cognitive deficits.[6,7] The term "continuation ECT" (C-ECT) has been used for ECT up to 6 months after an episode to prevent relapse (of the index episode), whereas "maintenance ECT" (M-ECT) aims to prevent recurrence of a new episode beyond 6 months. Despite the distinction between both C-ECT and M-ECT and relapse and recurrence, in this article, we will collapse the terms and only refer to M-ECT and relapse.

Tapering off the frequency of treatment sessions following an acute ECT course (e.g., weekly treatments for 4 weeks) is preferred over abrupt discontinuation.[8] This taper aims to reduce the risk of relapse in the critical first month post-ECT by allowing pharmacotherapy to exhibit the full clinical effect. Subsequently, it is appropriate to further decrease the frequency over the next months (e.g., biweekly for 8 weeks, and monthly for 2 months[9]). Alternatively, a protocol using rescue ECT treatments based on monitoring of symptoms and providing ECT treatments only in case of early signs of relapse can be used.[8,10]

The frequency and duration of M-ECT are usually tailored to the individual patient's needs. According to current practice recommendations, the continued need for M-ECT should be reassessed at least every 3 to 6 months.[11,12] If remission has been maintained for a relatively long period, an attempt can be made to discontinue M-ECT and monitor for symptom reemergence, providing rescue ECT treatments at early signs of relapse.[12] To date, there are no scientific data to inform clinicians about the duration of M-ECT. Moreover, little is known about the relapse rate after M-ECT discontinuation and the impact of patient and treatment characteristics on the risk of relapse. Three retrospective studies assessed the relapse rate following discontinuation of M-ECT and reported relapse rates between 18% and 44% at 6–8 months.[13-15] Moreover, diagnoses other than major depressive disorder (i.e., bipolar disorder, schizophrenia, and schizoaffective disorder), a higher number of previous episodes, and a shorter interval between M-ECT treatments (i.e., less than 1 month) were associated with increased risk of relapse after discontinuation of M-ECT.[13,14] In addition, a higher age and the presence of psychotic features have been suggested to be associated with decreased risk of relapse after a successful acute course of ECT for depression.[2,16] Since retrospective cohort studies often fail to detect less severe forms of relapse, for example, without the need for hospital admission, they tend to underestimate the true relapse rate. Also, it is difficult to determine the timing of relapse based on a review of medical records. Prospective studies are therefore needed to address these limitations.

The COVID-19 pandemic has prompted dramatic adjustments to the practice of ECT. At the start of the pandemic, its availability was limited because of relocation of anesthesiologists, risk of patient infection because of exposure to a healthcare setting, and implementation of time-demanding safety protocols related to the aerosol-generating nature of the procedure. As such, the majority of mental health centers in Flanders (Belgium) closed down their ECT units at the start of the pandemic.[17] In a limited number of centers, including ours, activity was maintained, albeit drastically reduced. In the context of the rapidly evolving pandemic, we were forced to make availability-related changes in ECT schedules and suspended M-ECT treatments in order to maintain capacity for the acute and severely ill. This highly unusual situation created an unexpected opportunity to study the course of illness in patients whose M-ECT treatment was discontinued abruptly.

Significant outcomes

- The 6-month relapse rate after abrupt discontinuation of M-ECT (44%) is comparable to the relapse rate following a successful acute course of ECT.
- Discontinuation of M-ECT may be considered, but caution is advised in patients with a diagnosis of psychotic disorder and those with a short interval between M-ECT treatments at the time of discontinuation.

Limitations

- The generalizability of our findings is limited by the relatively high mean age (69.46 years) of our cohort.
- The impact of maintenance pharmacotherapy on the risk of relapse was not assessed.

1.1 | Aims of the study

The aim of this study was to determine the 6-month relapse rate and time to relapse after abrupt discontinuation of M-ECT in a prospective manner and to assess the impact of clinical (i.e., age, diagnosis, indication, number of previous acute ECT courses) and M-ECT (i.e., total number of M-ECT treatments and M-ECT treatment interval at the time of discontinuation) characteristics on the risk of relapse.

2 | MATERIALS AND METHODS

2.1 | Participants and procedures

On 16 March 2020, all M-ECT treatments were put on hold at the ECT unit of the University Psychiatric Center KU Leuven in the context of the COVID-19 pandemic. All patients who had been receiving M-ECT up to this point in time were followed up prospectively for 6 months, or until relapse. M-ECT was considered the administration of ECT following an acute course at a frequency below twice a week. The indication for M-ECT was established according to international guidelines.[11,18] Therefore, all patients receiving M-ECT had shown significant clinical improvement during the index course. Either a Somatics Thymatron System IV device (Somatics, Lake Bluff, IL) or a MECTA spECTrum device (MECTA Corporation, Portland, ORE) was used, both during the index course and during M-ECT. Brief pulse (0.5 ms) right unilateral (or bitemporal in the most severely ill) ECT was administered twice a week. At the first treatment, the seizure threshold (ST) was established by empirical titration. Subsequent treatments were given at six times the ST. In the absence of significant clinical improvement after six to eight unilateral treatments, electrode placement could be switched to bitemporal at 1.5–2 times the ST. The dose administered and the electrode placement at the beginning of M-ECT were the same as at the end of the index course. M-ECT treatments were given weekly to once every 6 weeks. Treatment intervals were adjusted in a case-by-case manner according to clinical evaluation and interview with patients and their significant others. The pharmacologic regimen that was prescribed at the time M-ECT was stopped and was continued and monitored by the treating psychiatrist during the 6-month follow-up period (or until relapse).

2.2 | Data collection

Demographic and clinical data were collected from medical records: age (on 16 March 2020), gender, diagnosis (according to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association, 2013)),[19] indication for the index course, number of previous acute ECT courses (i.e., ECT administered at least twice weekly), number of ECT treatments during the index course, total duration of M-ECT and number of M-ECT treatments (from the first treatment with a frequency below twice weekly to the last M-ECT treatment before discontinuation because of the COVID-19 pandemic), interval between M-ECT treatments at the time of discontinuation, pharmacotherapy at the time of discontinuation (tricyclic antidepressant (TCA), lithium, selective serotonin reuptake inhibitor (SSRI), serotonin and norepinephrine reuptake inhibitor (SNRI), mood stabilizer or antipsychotic), and electrode placement at the time of discontinuation.

Patients were followed up for 6 months after the last M-ECT treatment. Their condition was assessed by their treating psychiatrist weekly to monthly, depending on the clinical picture. Relapse was defined as (i) hospital admission, (ii) restart of ECT, (iii) change of pharmacotherapy (i.e., either dose increase or new medication (apart from rescue medication, e.g., lorazepam or clotiapine for anxiety or insomnia)), (iv) completed suicide, or (v) suicide attempt, recorded by patients' treating psychiatrists using a standardized form. The date of relapse was the date of hospital admission, restart of ECT, change of pharmacotherapy, completed suicide or suicide attempt, whichever came first. If a patient was hospitalized and ECT was restarted on a later date, the date of admission was considered the date of relapse. This study was approved by the local ethical review board.

2.3 | Statistical analyses

Descriptive statistics were used to characterize the data. For categorical variables, frequencies and percentages were used; for continuous variables, means (standard deviation (SD)) or medians (interquartile range (IQR)) were used, as appropriate. We calculated the relapse rate and determined the time between the last M-ECT treatment and relapse. Patients with no recorded relapse during the observation period were censored at 6 months after the last M-ECT treatment. Cox proportional hazards models were fitted, including the following predictors: age (continuous), diagnosis (categorical), indication (categorical), number of previous acute ECT courses (continuous), number of M-ECT treatments (continuous), and interval between M-ECT treatments at the time of discontinuation (continuous). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the involved predictors were calculated. Patients were excluded from the analyses if their group consisted of only one participant: the patient with a diagnosis of autism spectrum disorder and the patient with a diagnosis of alcohol-induced major neurocognitive disorder were excluded from

the analyses with the variable diagnosis, and the patient with indication mania was excluded from the analyses with the variable indication. One patient, whose information on time to relapse was missing, was excluded from all time-to-event analyses. The significance level for the Cox proportional hazards analyses was defined as $p < 0.05$. We found no violations of the proportional hazards assumption. The data analysis for this manuscript was generated using SAS software, version 9.4 of the SAS System for Windows.

3 | RESULTS

3.1 | Patient and treatment characteristics

M-ECT was discontinued in a total of 83 patients. One patient was lost to follow-up, and another demanded a restart of M-ECT because of fear of relapse (without signs of symptom reemergence) during the 6-month observation period, yielding a final sample size of 81 patients (Figure 1). Table 1 shows the clinical and treatment characteristics of the 81 patients. The mean age was 69.46 (SD = 12.71) years. The indication for the index ECT course was major depressive episode with psychotic features ($N = 32$ (39.51%)), major depressive episode without psychotic features ($N = 31$ (38.27%)), psychosis (without concurrent major depressive episode or mania) ($N = 9$ (11.11%)), catatonia ($N = 8$ (9.88%)), or mania ($N = 1$ (1.23%)). DSM-5 diagnosis was major depressive disorder ($N = 51$ (62.96%)), bipolar disorder ($N = 16$ (19.75%)), psychotic disorder ($N = 12$ (14.81%)), autism spectrum disorder ($N = 1$ (1.23%)), or alcohol-induced major neurocognitive disorder ($N = 1$ (1.23%)). The median number of previous acute ECT courses was 1 (IQR =0, 2). The median duration of M-ECT was 58.71 weeks (IQR = 23.86, 98.00), and the median number of M-ECT treatments was 25 (IQR = 12, 47). The interval between M-ECT treatments at the time of discontinuation was weekly for 12 (14.81%), every 2 weeks for 18 (22.22%), every 3 weeks for 17 (20.99%), every 4 weeks for 9 (11.11%), every 5 weeks for 10 (12.35%), and every 6 weeks for 15 (18.52%) patients. All patients received concomitant pharmacotherapy with at least one drug at the time of M-ECT discontinuation.

3.2 | Relapse after abrupt discontinuation of M-ECT

Thirty-six (44.44%) patients relapsed within the 6-month observation period. As Figure 1 shows, the most frequent relapse event was restart of ECT ($N = 15$ (41.67%)), followed by hospital admission ($N = 12$ (33.33%)) and change of pharmacotherapy ($N = 9$ (25.00%)). We did not witness any completed suicides or suicide attempts. In the patients who relapsed, the median time to relapse was 8 weeks (IQR = 6.29, 13.00). The null hypothesis that all regression coefficients are zero was rejected for both the Cox proportional hazards model including diagnosis and the model including indication (diagnosis: $\chi^2 = 39.8288$, df = 6, $p < 0.0001$; indication: $\chi^2 = 39.7149$, df =7, $p < 0.0001$). The results of the Cox proportional hazards analyses in Table 2 indicate that patients with a diagnosis of psychotic disorder had a significantly higher risk of relapse compared to patients with a diagnosis of major depressive disorder as well as to patients with a diagnosis of bipolar disorder (Figure 2A). The risk of relapse was not significantly increased in patients with a diagnosis of bipolar disorder compared to patients with a diagnosis of major depressive disorder (Table 2; Figure 2A). Moreover, patients with indication psychosis had a significantly higher risk of relapse compared to patients with indication major depressive episode with psychotic features as well as to patients

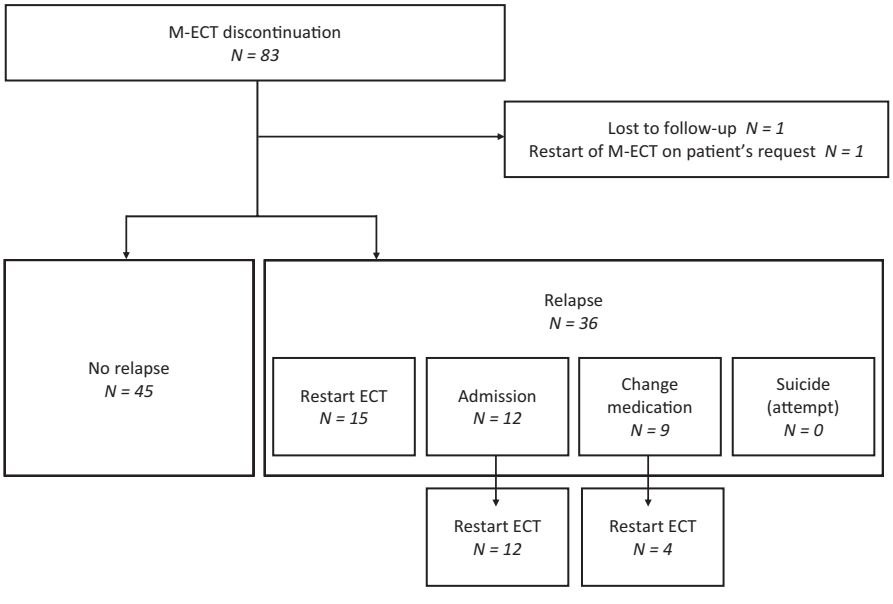

FIGURE 1 Flow diagram of patient selection, relapse event, and subsequent restart of ECT.

TABLE 1 Patient and treatment characteristics of included patients ($N = 81$)

Age (years), mean (SD)	69.46 (12.71)
Gender (female), *N* (%)	59 (72.84)
Diagnosis, *N* (%)	
Major depressive disorder	51 (62.96)
Bipolar disorder	16 (19.75)
Psychotic disorder[a]	12 (14.81)
Autism spectrum disorder	1 (1.23)
Alcohol-induced major neurocognitive disorder	1 (1.23)
Indication, *N* (%)	
Major depressive episode with psychotic features	32 (39.51)
Major depressive episode without psychotic features	31 (38.27)
Psychosis[b]	9 (11.11)
Catatonia	8 (9.88)
Mania	1 (1.23)
Number of previous acute ECT courses[c], median (IQR)	1 (0, 2)
Number of treatments during the index ECT course[d], mean (SD)	12.25 (6.91)
Total M-ECT duration (weeks), median (IQR)	58.71 (23.86, 98.00)
Number of M-ECT treatments, median (IQR)	25 (12–47)
M-ECT treatment interval[e], *N* (%)	
Weekly	12 (14.81)
Every 2 weeks	18 (22.22)
Every 3 weeks	17 (20.99)
Every 4 weeks	9 (11.11)
Every 5 weeks	10 (12.35)
Every 6 weeks	15 (18.52)
Pharmacotherapy[e,f], *N* (%)	
TCA	15 (18.75)
Lithium	15 (18.75)
SSRI	17 (21.25)
SNRI	22 (27.50)
Mood stabilizer	11 (13.75)
Antipsychotic	56 (70.00)
Electrode placement[e], *N* (%)	
Right unilateral	41 (50.62)
Bilateral	40 (49.38)

Abbreviations: SD, standard deviation; IQR, interquartile range; TCA, tricyclic antidepressant; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor.

[a]Schizophrenia: $N = 8$; schizoaffective disorder $N = 2$; schizophreniform disorder: $N = 1$; psychotic disorder because of another medical condition: $N = 1$.

[b]Without concurrent major depressive episode or mania.

[c]ECT administered at least twice weekly.

[d]Preceding M-ECT.

[e]At the time of M-ECT discontinuation.

[f]Information on pharmacotherapy was missing in one patient.

with indication major depressive episode without psychotic features (Table 2; Figure 2B). In addition, a greater number of previous acute ECT courses and a shorter interval between M-ECT treatments at the time of discontinuation were significantly associated with increased risk of relapse (Table 2). There was no significant effect of age and number of M-ECT treatments on the risk of relapse (Table 2).

Restart of ECT was the relapse event for 15 out of 36 (41.67%) patients. As Figure 1 shows, however, ECT was eventually restarted in all admitted patients ($N = 12$). Four of 9 (44.44%) patients required restart of ECT following change of pharmacotherapy. In total, ECT was thus restarted in 31 out of 36 (86.11%) patients.

4 | DISCUSSION

The COVID-19 pandemic created an unexpected opportunity to study the outcome of patients after abrupt discontinuation of M-ECT: 44% (36 out of 81) relapsed within 6 months. Although the 6-month relapse rate in our study is in line with the 44% relapse rate at 8 months in the retrospective cohort study by Huuhka et al.[13] ($N = 45$), Martínez-Amorós et al.[14] ($N = 73$) and Cabelguen et al.[15] ($N = 16$) reported noticeably lower 6-month relapse rates in their retrospective cohort studies: 18% and 22%, respectively. In these last two studies, patients were only included if M-ECT was given for a certain amount of time prior to discontinuation. This may have led to longer inter-treatment intervals at the time of M-ECT discontinuation and may have therefore caused relapse rates to be lower compared with our study, since a longer interval between M-ECT treatments at the time of discontinuation was associated with decreased risk of relapse in our study. Other factors may have contributed to the relatively high relapse rate in our study compared with the rates in the retrospective cohort studies. First, the decision to interrupt M-ECT in our sample was a case of *force majeure*, whereas in the retrospective studies, M-ECT cessation was based on clinical judgment (i.e., the patient being stabilized) or because of patients' refusal. Second, the prospective design of our study allowed us to detect relapses that were treated without the need for admission or restart of ECT (i.e., relapses that required change of pharmacotherapy). This type of relapse was not included in the definition of relapse in the retrospective cohort studies. Third, our study was conducted during the exceptionally stressing COVID-19 pandemic. The general stresses associated with a pandemic outbreak and reduced access to treatment can trigger a relapse.[20] Quarantine and lockdown, with loss of pleasurable activities and physical distancing reducing the availability of family and social support, seem to particularly affect people with pre-existing mental health problems.[21]

TABLE 2 Multivariable Cox proportional hazards models

Predictor	HR[a]	95% CI	*p*	Predictor	HR[a]	95% CI	*p*
Age	1.032	0.999, 1.066	0.0575	Age	1.028	0.994, 1.063	0.1024
Diagnosis				Indication			
• MDD vs. psychotic disorder	0.2606	0.1044, 0.6504	0.0040	• Catatonia vs. PD	2.7505	0.8046, 9.4024	0.1067
• BD vs. psychotic disorder	0.3322	0.1227, 0.8996	0.0302	• Catatonia vs. NPD	1.9902	0.5734, 6.9077	0.2784
• MDD vs. BD	0.7844	0.2913, 2.1122	0.6309	• Catatonia vs. psychosis	0.5311	0.1500, 1.8805	0.3266
				• PD vs. NPD	0.7235	0.2988, 1.7522	0.4733
				• PD vs. psychosis	0.1931	0.0726, 0.5133	0.0010
				• NPD vs. psychosis	0.2669	0.1012, 0.7038	0.0076
Number of previous acute ECT courses	1.530	1.193, 1.963	0.0008	Number of previous acute ECT courses	1.533	1.194, 1.969	0.0008
Number of M-ECT treatments	1.003	0.996, 1.010	0.3891	Number of M-ECT treatments	1.004	0.997, 1.011	0.2280
M-ECT treatment interval	0.566	0.433, 0.741	<0.0001	M-ECT treatment interval	0.508	0.384, 0.672	<0.0001

Abbreviations: 95% CI, 95% confidence interval; BD, bipolar disorder; HR, hazard ratio; MDD, major depressive disorder; M-ECT treatment interval, interval between M-ECT treatments at the time of discontinuation; NPD, major depressive episode without psychotic features; PD, major depressive episode with psychotic features.

[a]HRs greater than 1 indicate increased risk of relapse, HRs less than 1 indicate decreased risk.

Interestingly, the relapse rate after abrupt discontinuation of M-ECT in our study is in accordance with the rates following a successful acute course of ECT. In patients with unipolar or bipolar depression, 37.7% (95% CI = 30.7, 45.2%) relapsed within the first 6 months and 51.1% (95% CI = 44.7, 57.4%) by 12 months, despite treatment with continuation pharmacotherapy.[2] Likewise, in patients with schizophrenia, 12-month relapse rates range from 40% to 60%.[3] This finding of a similar relapse rate following discontinuation of M-ECT and termination of an acute course of ECT should be no surprise, since, in general, patients receiving M-ECT have had multiple, severe episodes, have failed to remain well on pharmacotherapy, and thus constitute a group that is prone to relapse. One may have expected the relapse rate in our sample to be even higher compared with the rates following a successful acute course of ECT, especially since M-ECT was discontinued without consideration of patients' condition in our study, whereas in studies on relapse following an acute course of ECT, termination is generally based on clinical judgment (i.e., when a patient has at least responded). Witnessing comparable relapse rates following an acute course of ECT and after discontinuation of M-ECT, one may generalize the advice to continue ECT after an acute course to patients in stable condition while on M-ECT: do not stop M-ECT thoughtlessly. Moreover, this finding underscores the importance of considering ECT as an essential medical procedure, especially in this COVID-era.[22] On the other hand, more than half of the patients remained well during the 6-month period following abrupt discontinuation of M-ECT. Clinicians may thus consider discontinuation of M-ECT in well-selected patients, but many patients will clearly need to continue.

In meta-analyses of placebo-controlled randomized trials including non-ECT treated patients with depressive disorders, bipolar disorder, or schizophrenia or schizophrenia-like psychoses, 6-month relapse rates after discontinuation of maintenance pharmacotherapy ranged from 34% to 52%.[23-25] Although it does not seem appropriate to compare these rates to the relapse rate in our study, since all patients received concomitant pharmacotherapy following M-ECT discontinuation and our sample consisted of so-called "difficult-to-treat" patients in which ECT and M-ECT were deemed necessary to achieve remission and prevent relapse, it adds to the evidence that patients are most vulnerable during the 6-month period after discontinuation of any successful treatment. In this period, close monitoring of early signs of relapse is of vital importance.

A greater number of previous acute ECT courses was associated with increased risk of relapse in our study (Table 2). This is consistent with the finding of Martínez-Amorós et al., who reported that patients with a greater number of previous episodes showed a higher risk of relapse after discontinuation of M-ECT.[14] In non-ECT treated samples of patients with major depressive disorder or bipolar disorder, the risk of relapse appears to increase with the number of episodes.[26] Likewise, the number of previous hospitalizations has been shown to be associated with relapse in patients with schizophrenia.[27] In our study, patients with a diagnosis of psychotic disorder were at increased risk of relapse, compared to both patients with a diagnosis of major depressive disorder and patients with a diagnosis of bipolar disorder (Table 2; Figure 2A). This is in line with the finding of a greater risk of relapse in patients with diagnoses other than major depressive disorder (i.e., bipolar disorder, schizophrenia and schizoaffective disorder) by Huuhka et al.[13] Moreover, patients with a shorter interval between M-ECT treatments at the time of discontinuation were at increased risk of relapse in our study (Table 2). This

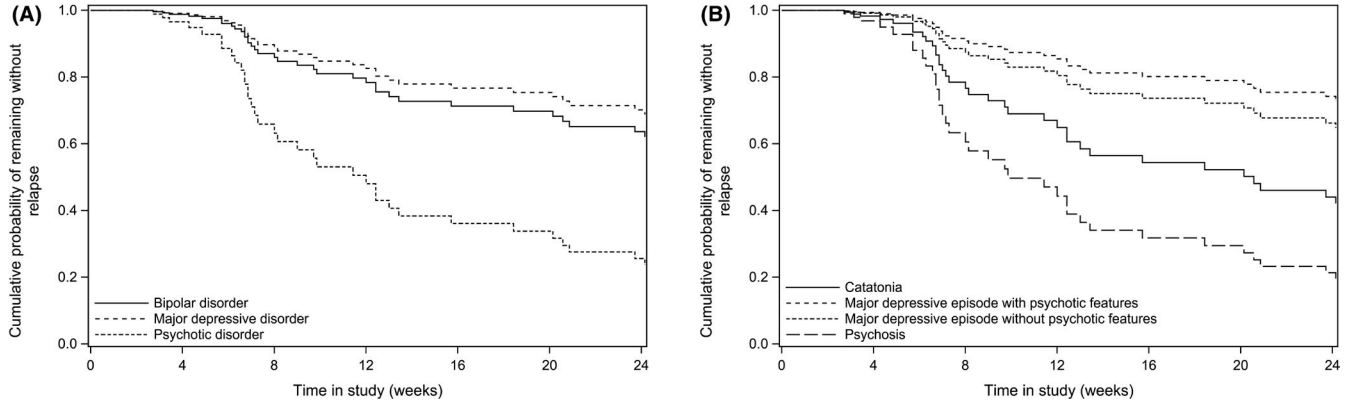

FIGURE 2 Relapse-free survival after abrupt discontinuation of M-ECT by (A) diagnosis and (B) indication. Multivariable-adjusted survival curves estimated with a Cox proportional hazards model.

is in keeping with the finding of Martínez-Amorós et al., who concluded that patients with an inter-treatment interval of less than 1 month showed a higher risk of relapse.[14] Presumably, in patients with a shorter interval between M-ECT treatments, the clinical improvement obtained after an acute course of ECT was not sufficiently consolidated at the time of discontinuation. This may implicate that before considering discontinuation of M-ECT, it would be advisable to ensure that sufficiently solid clinical stability has been achieved. Equivalent to a shorter inter-treatment interval being associated with increased risk of relapse, a greater interval seemed to protect against relapse in our sample. This finding provides support for current clinical practice recommendations suggesting that attempts should be made to space intervals out further if the patient remains well for a sustained period of time and that, if the patient has maintained remission for a relatively long duration, an attempt should be made to withdraw the M-ECT treatment and monitor progress closely, reinstituting M-ECT at early signs of relapse.[12] Although long-term M-ECT may provide the greatest chance of remaining well in some patients, the number of M-ECT treatments itself was not associated with relapse in our study.

In our sample, a higher age was not significantly associated with decreased risk of relapse. This may be because of the fact that our patients had a high mean age (69.46 years), while the studies reporting a decreased risk of relapse with higher age (after a successful acute course of ECT) included younger patients.[2] It has been suggested that patients with psychotic (late-life) depression are less likely to relapse after a successful acute course of ECT.[2,16] However, in our study, patients that started ECT for a psychotic depression did not have a lower risk of relapse, compared to patients with indication major depressive episode without psychotic features. Because of the naturalistic design, we did not have strict protocols during the follow-up period concerning maintenance pharmacotherapy. Therefore, the association between pharmacotherapy and relapse may have been confounded by unmeasurable factors and was therefore not assessed in this study.

4.1 | Limitations

The following limitations must be considered when interpreting the results of this study. First, although abrupt discontinuation of M-ECT is not an infrequent occurrence (e.g., in patients refusing further treatment), it is not "common practice," possibly limiting the generalizability of our findings. However, this abrupt cessation did eliminate the risk of bias that was present in the retrospective studies as part of the clinical decision-making process regarding discontinuation of M-ECT (i.e., either based on clinical judgment or because of patients' refusal). Second, since we studied a clinically treated population, observed effects may depend on other, unmeasured factors that correlate both with the exposure and outcome. We tried to limit this risk by including factors that are likely to affect the outcome in the multivariable Cox proportional hazards models. Third, we did not use a cutoff score on a standardized rating scale to define relapse. Nevertheless, hospital admission, restart of ECT, change of pharmacotherapy, and suicide (attempt) were used as robust indicators of a relapse. Finally, the generalizability of our findings is limited by the relatively high mean age of our cohort. Additional prospective studies including patients of all age-groups are needed to define the course of illness over a longer period of time and to assess the association between additional patient and treatment characteristics and relapse, such as symptom severity at the time of discontinuation and maintenance pharmacotherapy composition.

In conclusion, more than half of the patients remained well within 6 months following abrupt discontinuation of M-ECT. Also, almost half of the patients relapsed, similar to the relapse rate after an acute course of ECT. Patients with a shorter interval between M-ECT treatments at the time of discontinuation

seem to be at increased risk, as well as patients with a diagnosis of psychotic disorder compared to patients with mood disorders. These patient and treatment characteristics can aid in the decision-making process when considering discontinuation of M-ECT. In case M-ECT is stopped, close monitoring should be ensured to detect early signs of relapse.

CONFLICTS OF INTEREST

The authors report no conflict of interest.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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