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## **Adherence to treatment guidelines in clinical practice for using electroconvulsive therapy in major depressive episode**

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## **Abstract**

**Background:** ECT is the most effective treatment of major depressive episode (MDE) but remains a neglected treatment. The French Society for Biological Psychiatry and Neuropsychopharmacology aimed to determine whether prescribing practice of ECT followed guidelines recommendations.

**Methods:** This multicenter, retrospective study included adult patients with major depressive disorder (MDD) or bipolar disorder (BD), who have been treated with ECT for MDE. Duration of MDE and number of lines of treatment received before ECT were collected. The reasons for using ECT, specifically first-line indications (suicidality, urgency, presence of catatonic and psychotic features, previous ECT response, patient preference) were recorded. Statistical comparisons between groups used standard statistical tests.

**Results:** Seven hundred and forty-five individuals were included. The mean duration of MDE before ECT was 10.1 months and the mean number of lines of treatment before ECT was 3.4. It was significantly longer for MDD single episode than recurrent MDD and BD. The presence of first-line indications for using ECT was significantly associated to shorter duration of MDE (9.1 vs 13.1 months,  $p < 0.001$ ) and lower number of lines of treatment before ECT (3.3 vs 4.1,  $p < 0.001$ ).

**Limitations:** This is a retrospective study and not all facilities practicing ECT participated that could limit the extrapolation of the results.

**Conclusion:** Compared to guidelines, ECT was not used as first-line strategy in clinical practice. The presence of first-line indications seemed to reduce the delay before ECT initiation. The improvements of knowledge and access of ECT are needed to decrease the gap between guidelines and clinical practice.

**Key words:** Electroconvulsive therapy, clinical guidelines, major depressive episode, major depressive disorder, bipolar disorder

## **1. Introduction**

Electroconvulsive therapy (ECT) represents for nearly 80 years in psychiatry an appropriate and effective treatment for a number of psychiatric indications, specifically in mood disorders. ECT has been reported to induce a prompt improvement in symptoms of depression in the majority of adult patients treated with an estimated remission rate of 65% to 75% (Bahji et al., 2019; Lisanby, 2007; Pagnin et al., 2004; UK ECT REV Group, 2003). Although ECT is the most acutely effective treatment in depression, it remains a neglected and underused treatment (Eranti and McLoughlin, 2003; Leiknes et al., 2012; Sienaert et al., 2016). ECT is frequently regarded as a therapeutic strategy for patients severely resistant to medication. Moreover, ECT practice may be different between countries or between physicians within the same country. This clinical practice can lead to different clinical outcomes and rates of cognitive impairments (Kellner et al., 2016; Kolar, 2017; Sackeim et al., 2007).

International clinical guidelines do not limit their recommendations to the use of ECT as a third-line treatment or more for depressed patients who have not responded to adequate trials of medication and psychotherapy (Bayes et al., 2018; Malhi et al., 2015; Milev et al., 2016; Weiss et al., 2019). ECT should also be considered as a first-line treatment when rapid clinical improvement is required and when patient preference or previous response to ECT are reported.

Among all available treatments for the management of major depressive episode (MDE) in major depressive disorder (MDD) or bipolar disorder (BD), guidelines recommend ECT as a first-line therapeutic strategy in some clinical situations: high suicidality, presence of psychotic or catatonic features, urgency (e.g. poor oral intake), previous positive response to ECT and in case of patient preference (Bayes et al., 2018; Malhi et al., 2015; Milev et al., 2016; Weiss et al., 2019).

To our knowledge, no study has been performed to assess the level of adherence to treatment guidelines in clinical practice concerning the use of ECT for the management of MDE in MDD and BD.

In this context, the French Society for Biological Psychiatry and Neuropsychopharmacology (AFPBN, [www.afpbn.org](http://www.afpbn.org)) carried out a study to determine whether prescribing practice of ECT followed guidelines recommendations. Specifically, we sought to determine the duration of MDE and the number of lines of treatment before the initiation of ECT according to the presence or absence of first-line indications for using ECT from guidelines.

## **2. Methods**

### **2.1. Study design and recruiting network characteristics**

This multicenter, retrospective, cross-sectional study included patients recruited by the French national network of 12 expert and collaborative centers hosted by academic departments of psychiatry (Besançon, Brest, Clermont-Ferrand, Créteil, Grenoble, Lyon, Marseille, Montpellier, Nantes, Paris, Toulouse, Tours). This network was set up by the FondaMental Foundation ([www.fondation-fondamental.org](http://www.fondation-fondamental.org)) and funded by the French Ministry of Research and the French Ministry of Health to improve the diagnosis, assessment and management of psychiatric disorders, including MDD and BD (Henry et al., 2011; Yroni et al., 2017).

The study was carried out in accordance with ethical principles for medical research involving humans (WMA, Declaration of Helsinki). The assessment protocol was approved by the relevant ethical review board (CPP Sud-Est VI, 2016 / CE 07). All data were collected anonymously.

## 2.2. Participants

The study included all patients over 18 years with MDD or BD, who have received ECT as acute treatment for a MDE according to DSM-IV-TR criteria from 1 January 2009 to 1 January 2014.

Exclusion criteria were schizophrenia or autistic spectrum and schizoaffective disorder diagnosis according to DSM-IV-TR criteria.

## 2.3. Measures

The following data were extracted from the computerized or paper clinical records: sociodemographic data (age, gender, socioeconomics characteristics), lifetime diagnosis (MDD single episode, recurrent MDD, BD type 1 and 2), substance use disorders (tobacco, alcohol, cannabis, opioids, psychostimulants) and chronic physical disease comorbidities (cardiovascular, respiratory, neurologic, neoplastic, infectious, systemic, endocrinal and metabolic).

Duration of MDE (delay between the onset of the episode and the first day of ECT) and the number of lines of treatment received consecutively (in monotherapy or in combination) before the initiation of ECT were collected.

The reasons for using ECT as previously described, specifically first-line indications based on international guidelines (high suicidality, urgency (severe depression associated with insufficient oral intake), presence of catatonic and psychotic features, previous ECT response, patient preference), were also recorded. The only one French guideline from the National Authority for Health for the use of ECT has not been considered because it was out of date and did not offer any recommendation grades based on the clinical characteristics of the MDE (ANAES, 1997).



## 2.4. Statistical analysis

Sociodemographic and clinical data are presented as the mean (SD) for continuous variables and frequency distribution for categorical variables.

Statistical comparisons between groups of patients were done by using standard statistical tests: the Chi-square test for categorical variables and Student t test, Anova test or Mann-Whitney test depending on the number and the distribution for continuous variables.

Analyses were conducted using SAS 9.3 (SAS Statistical Institute, Cary, North Carolina). All statistical tests were 2-tailed, with the  $\alpha$  level set at .05.

## 3. Results

We identified 878 patients who initiate ECT for treatment of MDE according to DSM-IV-TR criteria between 1 January 2009 and 1 January 2014. Of these, 133 (15.1%) were excluded from analyses because diagnosis, duration of MDE before the initiation of ECT and reasons for using ECT were missing or not available in medical records.

The demographic and clinical characteristics of included patients are presented in Table 1.

The mean duration of MDE before ECT was 10.1 months (Table 2). It was significantly longer for MDD single episode (14.5 months), than recurrent MDD (10.6 months) and BD (7.8 months,  $p<0.001$ ). It also was shorter in case of catatonic features (6.7 months,  $p<0.006$ ) and psychotic features (8.6 months,  $p<0.05$ ). The mean number of lines of treatment before the initiation of ECT was 3.44. Significant differences between centers on the duration of MDE ( $p<0.001$ ) and the number of lines of treatment ( $p<0.001$ ) before ECT were found (see Table S1 in the supplementary material).

The presence of first-line indications for using ECT from guidelines was significantly associated to shorter duration of MDE before the initiation of ECT (9.1 vs 13.1 months,  $p < 0.001$ , Figure 1 part A), more specifically, the presence of catatonic and psychotic features, previous response to ECT and urgency (Table 3).

Similarly, the presence of these first-line indications was also associated to lower number of lines of treatment before the initiation of ECT (3.3 vs 4.1,  $p < 0.001$ , Figure 1 part B). The previous response to ECT and the urgency had significantly lower number of lines of treatment before the initiation of ECT (Table 3). Number of lines of treatment did not differ with respect to the presence of high suicidality, catatonic or psychotic features and patient preference.

#### **4. Discussion**

To our best knowledge, this is the first study assessing the level of adherence to treatment guidelines in clinical practice for using ECT in the management of MDE in MDD and BD. We found a mean duration of MDE before the initiation of ECT of about 10 months and between 3 and 4 lines of treatment received before the first ECT session. The duration of MDE before ECT was significantly longer for MDD single episode than recurrent MDD and BD. The presence of first-line indications for using ECT from guidelines seemed to reduce the duration of MDE before the initiation of ECT, specifically, in case of catatonic and psychotic features, previous response to ECT and urgency. Finally, the presence of these first-line indications (mainly the previous response to ECT and the urgency) was also associated to lower number of lines of treatment before the initiation of ECT.

Our results were consistent with the international treatment guidelines in clinical practice for using ECT in the management of MDE, highlighting the need for using ECT earlier in case of

psychotic or catatonic features, urgency (e.g. poor oral intake), previous positive response to ECT (Bayes et al., 2018; Malhi et al., 2015; Milev et al., 2016; Weiss et al., 2019). Indeed, ECT is the highest effective treatment for catatonia (Luchini et al., 2015; Medda et al., 2015) and psychotic features (Petrides et al., 2001) with generally early response. However, if the international treatment guidelines recommend using ECT as a first-line therapeutic strategy in these clinical situations, the initiation of ECT in clinical practice seemed to be tried only after at least 3 lines of treatment.

Unexpectedly, the presence of suicidal risk and the patient preference for ECT were not associated with a significant reduction in the MDE duration. Nevertheless, ECT may provide quick and reliable relief of suicidal intent and reduction of suicide risk with high rates of success (Fink et al., 2014; Youssef et al., 2019). The limited literature on the effect of ECT on suicidality and the available evidence for psychotherapies (ie. cognitive behaviour therapy) and drug interventions (ie. antidepressants, lithium) on the reduction of suicide ideations or suicide attempts could partly explain our results (Melhum et al., 2006). Taking into account the patient preference is part of a process of shared decision-making and is now a general way to plan treatment, particularly for ECT, in MDD or BD (Samalin et al., 2018). We can assume that the patient preference for ECT could occur after other therapeutic strategies failed and explain the delay to initiate ECT treatment.

In the total sample, we found a long duration between the beginning of MDE and the beginning of ECT. This is a major concern because the duration of MDE has a negative prognostic impact depending on the neuroprogression of the disease in terms of plasticity loss, atrophy and functional/cognitive impairment (Belleau et al., 2019; Maes et al., 2019).

This duration could be affected by the negative patient attitudes towards ECT, the psychiatrist's choice/practice and by the access delay to ECT.

First, socio-cultural and economic factors and the earlier misuse of ECT during the Nazi era may have contributed to the media and public misperceptions of ECT (Gazdag and Ungvari, 2019). Patients who have not received ECT are more likely to derive their knowledge and attitudes about ECT from media sources. High proportion of these patients has negative perception of ECT (Dan et al., 2014). However, longitudinal studies showed that patient attitudes become more positive following the experience of the ECT treatment (Aoki et al., 2016). Consequently, we can assume that the duration of MDE before ECT could be affected by the delay of ECT acceptance of patients who have not experienced this treatment.

Second, even if this is less frequent over the last decade, it could, still, occur some stigma about ECT and concerns about its potential cognitive adverse effects from physicians (Dowman et al., 2005; Sackeim et al., 2007). Moreover, it seemed that there was a lack of knowledge and teaching about ECT (Blaj et al., 2007; Culas et al., 2003; Sienaert et al., 2016). Even if some countries, as Scotland, have a set of essential standards for induction for professionals administering ECT: i. Trainee doctors receive theoretical training in ECT, ii. Trainee doctors receive practical demonstration before delivering ECT and iii. Trainee doctors are supervised for a minimum of 3 sessions before administering ECT without direct supervision (Scott and Semple, 2018), it is not the case in most western countries. Despite academic degree available for practitioners in France (a national university degree on the practice of ECT and targeted training offered by the Non Invasive Brain Stimulation section of the AFPBN, [www.afpbn.org/sections/step](http://www.afpbn.org/sections/step)), no academic training is required in France for the practice of this treatment. Except psychiatrists with extensive experience or working in ECT unit, most physicians seem to prefer testing a third or fourth lines of drug treatment. Finally, the delay of access to ECT may also partly explain the duration of the MDE before the initiation of ECT. No data in the literature concerning the time required to access ECT in France is available. However, due to the significant differences between centers in the

duration of MDE before ECT, it appears that this accessibility may vary from one institution to another. Worldwide large global variation was found in ECT utilization, administration, and practice highlighting a need for improving the access to ECT and sharing of knowledge about ECT and learning from each other's experiences (Leiknes et al., 2012; Lin et al., 2019; Sanz-Fuentenebro et al., 2017). More generally, health care systems should pay more attention to neuromodulation techniques (ie. ECT, repetitive transcranial magnetic stimulation or transcranial direct current stimulation) in view of their promising therapeutic results (Sauvaget et al., 2018). Specific centers with specialized teams should be developed and integrated in official networks, particularly to enhance the access to ECT as well as other neuromodulation techniques.

In our sample, the mean age was 61.3 and over half of patients treated with ECT had chronic physical comorbidities. These data were consistent with literature about age and chronic physical comorbidities. Indeed, different surveys suggested that about one fourth to half of the patients receiving ECT were aged above 65 years (Chanpattana, 2007; Geduldig and Kellner, 2016; Grover et al., 2018; Prudic et al., 2001; Reid et al., 1998; Wood and Burgess, 2003). It seemed that there were 2 to 7 times more likely to receive ECT, compared to subjects belonging to other age groups (Duffett et al., 1999; Olfson et al., 1998). ECT efficacy may be superior in the elderly compared to younger adults with a faster therapeutic effect (Spaans et al., 2016). In addition, ECT is considered as a low-risk treatment for patients with medical disorders (Grover et al., 2018; Kelly and Zisselman, 2000) including neurodegenerative disorders (Oudman, 2012)

### ***Limitations***

There are some limitations to this study. This is a retrospective study with potential bias in data collection. More specifically, some missing data in the clinical records could underestimate the mean number of lines of treatment before the initiation of ECT.

Not all facilities practicing ECT in France participated to this study. This could limit the extrapolation of the results.

## **5. Conclusion**

We highlighted an important duration of MDE before the initiation of ECT. Compared to international guidelines, ECT was not used as first-line strategy in clinical practice. However, the presence of first-line indications to use ECT from guidelines seemed to reduce the delay before the initiation of ECT.

The improvement of knowledge of practice of ECT from psychiatrists (and residents), the development of accreditation procedures for ECT units and enhancing the access to ECT by supporting creation of specific psychiatric neuromodulation units, are needed to decrease the gap between international guidelines and clinical practice and improve MDE care.

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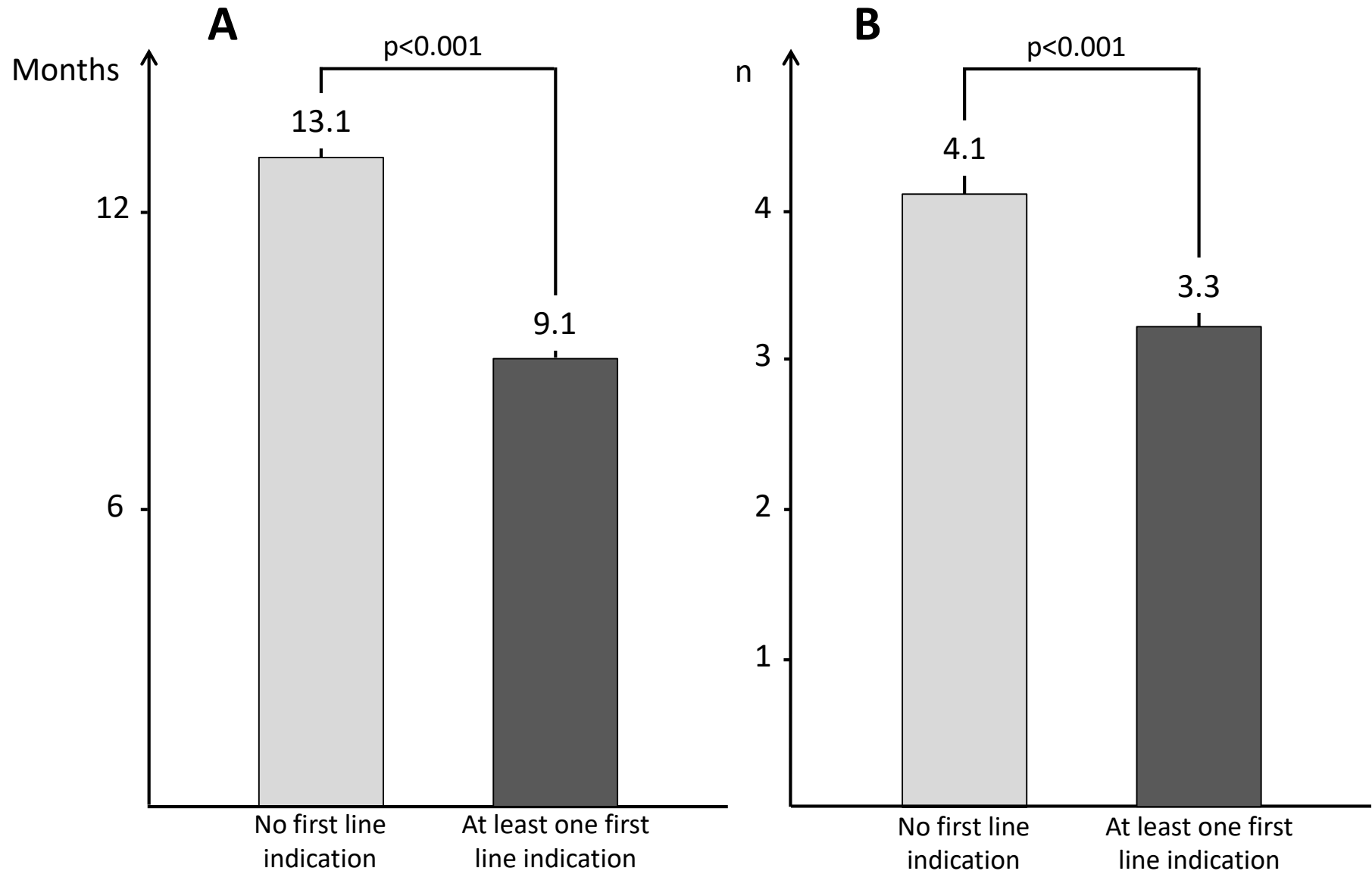
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Figure 1. Comparisons according the presence or absence of at least one first line indications for using ECT in guidelines



A. Mean duration of MDE before ECT; B. Mean number of lines of treatment before ECT

**Table 1.** Socio-demographic and clinical characteristics of the sample

Characteristics		Mean (SD) or n (%)
<i>Sociodemographic</i>		
Age (years)		61.27 (15.01)
Gender	Males	252/745 (33.83)
Employment status	Employment	159/713 (22.3)
<i>Clinical</i>		
Lifetime diagnosis	MDD single episode	109/745 (14.63)
	MDD recurrent	360/745 (48.32)
	Bipolar disorder	276/745 (37.05)
Characteristics of the episode	Psychotic features	310/745 (41.61)
	Catatonic features	52/745 (6.98)
	Melancholic features	452/745 (60.67)
	Atypical features	21/745 (2.82)
	No features	220/745 (29.53)
Comorbidities	Chronic medical disease	454/737 (61.60)
	Substance use disorder	
	Tobacco	128/704 (19.34)
	Alcohol	56/736 (7.61)
	Cannabis, opioid, psychostimulant	81/737 (11.00)

*MDD: major depressive disorder; SD: standard deviation. Values are given as mean (SD) or as n (%) of patients.*

**Table 2.** Duration of episode before ECT according to lifetime diagnosis, characteristics of the episode and comorbidities

	Mean duration of episode before ECT (months)	p-value
<i>Total sample</i>	10.11 (12.85)	
<i>Lifetime diagnosis</i> <sup>1</sup>		
MDD single episode	14.5 (10.05)	< 0.001
MDD recurrent	10.55 (13.99)	
Bipolar disorder	7.79 (10.17)	
<i>Characteristics of the episode</i> <sup>2</sup>	Absent                      Present	
Psychotic features	11.17(14.24)                      8.61(10.45)	0.005
Catatonic features	10.36 (13.08)                      6.68 (8.68)	0.006
Melancholic features	10.86 (13.98)                      9.61 (12.05)	0.209
Atypical features	9.91 (12.00)                      16.81 (29.85)	0.303
No features	9.61 (13.01)                      11.28 (12.41)	0.105
<i>Comorbidities</i> <sup>2</sup>	Absent                      Present	
Substance use disorder	9.89 (12.89)                      11.27 (12.95)	0.283
Chronic medical disease	9.62 (10.67)                      10.51 (14.11)	0.332

Values are given as mean (SD)

MDD: major depressive disorder; SD: standard deviation

<sup>1</sup> Anova-test

<sup>2</sup> T-test



**Table 3.** Comparisons according the presence or absence of first line indications for using ECT in guidelines

<i><b>First line indications for using ECT</b></i>	n (%)	<b>Mean duration of episode before ECT (months)</b>			<b>Mean number of lines of treatment before ECT (n)</b>		
		Absent	Present	p-value	Absent	Present	p-value
High suicidality	125 (16.78)	10.17 (13.12)	9.78 (11.48)	0.761	3.41 (2.30)	3.57 (2.11)	0.483
Urgency	210 (28.19)	10.78 (12.95)	8.37 (12.44)	0.021	3.73 (2.34)	2.76 (1.90)	<0.001
Previous ECT response	174 (23.36)	11.29 (13.56)	6.20 (9.17)	<0.001	3.66 (2.27)	2.78 (2.11)	0.001
Catatonic features	52 (6.98)	10.36 (13.10)	6.68 (8.68)	0.006	3.47 (2.29)	2.96 (1.78)	0.072
Psychotic features	310 (41.61)	11.17 (14.24)	8.61 (10.45)	0.005	3.58 (2.30)	3.24 (2.20)	0.063
Patient preference	61 (8.19)	9.74 (11.95)	14.22 (20.12)	0.091	3.40 (2.26)	3.77 (2.24)	0.240

*Values are given as mean (SD)*

*SD: standard deviation*