# Analysis of indications for electroconvulsive therapy in the hospitalized psychiatric patients

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UNIVERSITY OF ZAGREB

SCHOOL OF MEDICINE

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# Analysis of Indications for Electroconvulsive Therapy in the Hospitalized Psychiatric Patients

**GRADUATION THESIS**


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Part of the results of this thesis has been presented as an e-poster at the 25th European Congress of Psychiatry, from 1st till 4th of April 2017, in Florence, Italy.

List of Abbreviations

| Abbreviation | Explanation |
|---|---|
| BAD | Bipolar Affective Disorder |
| CPK (CK) | Creatine Phosphokinase (Creatine Kinase) |
| DSM-5 | Diagnostic and Statistical Manual of Mental Disorders 5th edition |
| ECT | Electroconvulsive therapy |
| EST | Electrostimulative therapy |
| ENMT | Electroneuromodulative therapy |
| GABA | Gamma-aminobutyric acid |
| ICD-10 | International Statistical Classification of Diseases and Related Health Problems 10th Revision |
| MAOI | Monoamine oxidase inhibitors |
| MDD | Major depressive disorder |
| MDE | Major depressive episode |
| NA | Noradrenaline or norepinephrine |
| NMS | Neuroleptic Malignant Syndrome |
| SAD | Schizoaffective disorder |
| SSRI | Selective Serotonin Reuptake Inhibitors |
| TCA | Tricyclic antidepressant |
| WHO | World Health Organization |
| 5-HT | 5-hydroxytryptamine or serotonin |

**CONTENTS**

**SUMMARY**

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**Analysis of indications for electroconvulsive therapy in the hospitalized psychiatric patients**

All around the world guidelines and indications for electroconvulsive therapy (ECT) differ. However, ECT is considered the most effective in treating depression, schizophrenia, mania, suicidality, and treatment resistance. The goal of this research was to analyze ECT indications from medical history of the hospitalized patients in the time period 2010-2017. There were 213 patients treated with ECT, previously diagnosed with schizophrenia, depression or bipolar disorder. The leading ECT indication was treatment resistance associated with already mentioned diagnoses, followed by suicidality, catatonia and neuroleptic malignant syndrome. Men were significantly younger than women receiving the first ECT treatment and more often they had resistant positive schizophrenia symptoms. Women more often had negative resistant schizophrenic symptoms and mood disorders as an indication. Within one year after receiving ECT, 1/3 of the patients were rehospitalized without differences in indications. Therapy resistance is gaining more importance as an ECT indication. Further studies will provide a better insight into ECT as a treating method, better understanding of the treatment, targeted and timely set indications as well as neutralization of controversies around ECT.

**Keywords**: ECT, indications for ECT, pharmacotherapy resistance, psychosis, suicidality

**SAŽETAK**

Ana Stručić

**Analiza indikacija za elektrokonvulzivnu terapiju u hospitaliziranih psihijatrijskih bolesnika**

Diljem svijeta smjernice i indikacije za elektrokonvulzivnu terapiju (EKT) variraju, a EKT se smatra učinkovitim u liječenju depresije, shizofrenije, manije, suicidalnosti i terapijske rezistencije. Cilj ovog istraživanja bio je analizirati indikacije za EKT u hospitaliziranih bolesnika u periodu od 2010. do 2017. godine iz medicinske dokumentacije. Liječenje EKT-om primilo je 213 bolesnika s dijagnozom shizofrenije, depresije ili bipolarnog poremećaja. Vodeća indikacija za aplikaciju EKT-a bila je terapijska rezistencija povezana s navedenim dijagnozama, a rjeđe suicidalnost, katatonija i maligni neuroleptički sindrom. Muškarci su bili značajno mlađi od žena prilikom prve aplikacije EKT-a, i češće su imali indikaciju rezistentnih pozitivnih simptoma shizofrenije. Bolesnice su češće imale indikaciju rezistentne negativne shizofrenije i poremećaja raspoloženja. Unutar godine dana nakon EKT-a, ponovo je hospitalizirana trećina bolesnika, bez razlika između indikacija. Terapijska rezistencija dobiva sve veći značaj kao indikacija za liječenje EKT-om, uz tradicionalne primarne indikacije. Istraživanja primjene EKT-a u liječenju psihičkih bolesti omogućit će bolje razumijevanje ove metode liječenja, ciljano i pravovremeno postavljanje indikacija, te smanjivanje kontroverzi povezanih s ovom metodom liječenja.

**Ključne riječi**: EKT, indikacije za EKT, rezistencija na psihofarmake, psihoza, suicidalnost

## INTRODUCTION

Electroconvulsive therapy (ECT) is a method of treatment that cannot dispose of the negative connotation thanks to the controversial past, the spread of disinformation and the ignorance that is still present to this day among the nonprofessionals, as well as among the professionals. In order to create a gap between past and present, and to get the term ECT destigmatized, some new terms are introduced: electrostimulative therapy (EST) or electroneuromodulative therapy (ENMT) (1).

At the time the ECT was discovered, it was believed that epileptic seizures prevent schizophrenia and that people who had suffered from seizures were in some way protected against schizophrenia. In 1933, while the young Hungarian psychiatrist and neuropathologist Lasislas von Meduna worked at the Budapest Psychiatric Investigation Institute, he noticed antagonistic activity between these two diagnoses – psychotic patients had fewer epileptic seizures, and patients with diagnosed epilepsy had fewer psychoses (2). Based on this, he concluded that an artificially induced epileptic attack could have a preventive effect, namely treat schizophrenia. He started testing drugs that cause convulsions: first on animals, and then on humans. The best results were obtained by experimenting with intravenous injection of metrazole (3). In 1937, Ugo Cerletti, a neurologist, while observing the "anesthesia" of pigs in the slaughterhouse, realized that an epileptic seizure could be triggered in a different way – by conducting electricity through the patient's body, just as the butchers did to the pigs. After many attempts and numerous experiments on animals, in April 1938, in collaboration with Luci Bini, the ECT was first used on a human being (4). It was a patient diagnosed with schizophrenia and accompanying delusions, hallucinations and confusion, and series of electroshocks improved his condition. Throughout the following years, ECT has expanded throughout the world and has become one of the ways to treat symptoms, often in problematic patients.

ECT is as a therapeutic method very effective, although the mechanism of action is not fully clear. There are many theories (diencephalon massage theory, dissolution and reconstruction theory, reconnection theory, etc.) that are still not proven, however we can say with certainty that ECT truly changes the function of different neurotransmitter systems: serotonergic, 5-HT (increase in postsynaptic 5-HT receptors, changes in postsynaptic regulation of 5-HT release), GABA (decreased synthesis and release), endogenous opiates (increase of the activity),

noradrenergic, NA (down-regulation postsynaptic β receptors), acetylcholine (down-regulation of muscarinic receptors) (1).

We can distinguish two methods of treatment with ECT: according to the position of the electrodes (unilateral and bilateral) and according to the performance (native and nonconvulsive) (1). Native ECT is outdated, unethical, and is no longer used. The nonconvulsive or mitigated ECT i.e. the ECT we know today is not so dramatic (1). It is initiated by the administration of thiopental (short-acting barbiturate) and succinylcholine (muscle relaxant), which prevents *grand-mal* seizures in the conduction of electric current through the patient's body and thus spinal or long bone fractures (5). Barbiturates and muscle relaxants prevent blood pressure increase and tachycardia, and excessive bronchial secretion induced by *n. vagus* is avoided by atropine (5). Performing an electrical current of 200 to 1600 mA in the body of the patient per application lasts only 0.1 to 0.5 s, and the therapeutic effect requires a current of 70 to 130 V (1). The ECT is applied in cycles of 12-15 applications, such as intermittent therapy or maintenance therapy (e.g. once a month). There are certain diseases and conditions in which it is highly recommended or strictly forbidden to implement ECT, such as: implanted cardiac electrostimulation device, myocardial infarction, cardiac arrhythmia, unregulated hypertension, abdominal aorta aneurysm, cerebral aneurysm, fresh cerebral hemorrhage, elevated intracranial pressure, brain tumor, acute respiratory infection (5).

Indications for which ECT is recommended are depression, schizophrenia, mania, suicidality, resistance to therapy. Generally, indications can be categorized into ECT as the first line of therapy, second line of therapy and so-called "last-resort" therapy (6). The first line of therapy includes cases of febrile catatonia, neuroleptic malignant syndrome (NMS), major depressive episode, schizoaffective psychosis, schizophrenia and life-threatening, pharmacologically caused adverse effects. The second line of therapy implies failure of depression treatment with conservative methods, schizoaffective psychosis, schizophrenia, mania, depression and psychotic symptoms of organic etiology. ECT as the "last-resort" therapy involves cases of therapeutic resistance and in some areas – obsessive-compulsive syndrome, dyskinesia, Gilles de la Tourette syndrome, epilepsy, Parkinson's disease. Nowadays, in developed countries, the most frequent indication for ECT is depression. Other indications are mainly mania and schizophrenia (7). Regardless of the indication, it is necessary to obtain an informed consent from the patient. If due to the nature of the illness, the patient is unable to give an informed

consent (catatonia, stupor, mania, acute paranoid conditions), then it is possible to obtain consent from by the law assigned caregivers (6).

As with other medical procedures, there are some complications and unpleasant side effects with ECT as well. The most common are confusion, delirium, temporary headache, muscle ache, vomiting, tooth injuries, circulatory collapse, and prolonged convulsions (8). The most important are the cognitive side effects that can be divided into postictal disorientation or confusion, anterograde amnesia, retrograde amnesia, and cognitive adverse effects not connected with memory (9). Postictal confusion does not last long and therefore does not represent a significant clinical problem, while the anterograde amnesia may last for a couple of weeks or even months, and the retrograde amnesia about autobiographical data may potentially be a lasting consequence of the ECT (10). Cognitive side effects usually depend on factors such as the application site, the amount of electrical energy the patient will receive, and the frequency of the application (11), so that the unwanted effects can be reduced by using short or ultrasound stimulation and the right unilateral instead of bilateral application or bitemporal convulsion (12). ECT is considered to be a therapy of extremely low morbidity and mortality. Fatalities are only 2-4.5 per 100,000 performed procedures, which can be compared with the risk of anesthesia during small surgeries (13). Every patient who is about to receive ECT must be familiar with the benefits of this therapy and the potential consequences.

The primary purpose of the ECT was to cure or at least to relieve ailments of schizophrenia. Thus, ECT was a standard for treating schizophrenia up to 1950s until it was overshadowed by more effective antipsychotics (14). Schizophrenia is the most known chronic psychiatric disorder affecting approximately 24 million people around the world (15). It is a psychotic disorder that disturbs the mind, mood, behavior, and/or personal relationships, leaving devastating consequences on the individual and his family (16) and significantly damages the person's functionality and his quality of life, causing various forms of disability. The frequency of schizophrenia in the general population is 1%, affecting men and women equally. The first psychotic episode usually occurs in late teenage years and early twenties or even thirties (16). Men are mostly affected in the early age and women later in life. The symptoms of schizophrenia can be divided into positive, negative and cognitive. Positive symptoms include hallucinations, most commonly hearing delusions, unorganized thinking, and unorganized psychomotor behavior (catatonia) (16). They are the most common in the acute phase of the disease and are very recognizable. Negative symptoms are flat affect

(difficulty in showing and experiencing feelings), avolition (lack of motivation), social retreat, alogia (poverty of speech), anhedonia (inability to experience satisfaction and enjoyment in life), and concentration problems (15). These symptoms contribute to patient's inconspicuousness and are in fact the cause of the lack of quality social interaction. Cognitive symptoms include disturbances of attention, memory and abstract thinking, which are responsible for the dysfunction of a schizophrenic patient in their daily lives (15). Because of these symptoms, the patients can not plan their daily lives, their actions are not subject to any logic, and cannot logically infer or distinguish essential from irrelevant and have memory, attention, concentration, and executive functions. In this division, positive, negative and cognitive symptoms may include depressive symptoms (15). They are related to mood of the patient and are the main culprit for suicide attempts.

Schizophrenia can be divided into several clinical types characterized by predominant symptoms: a paranoid-hallucinatory type characterized by paranoid delusional ideas, auditory hallucinations and hypochondriac delusional ideas, a hebephrenic (disorganized) type dominated by depersonalization and derealization phenomena, a catatonic type specific for hypo or hyperkinetic phenomena and simplex type – chronic, agonizing, late-recognizable, which most often has an unfavorable outcome (15). Diagnostic criteria are summarized in two contemporary psychiatric classifications: International Classification of Diseases and Related Health Problems, 10$^{th}$ revision (ICD-10) (16) and Diagnostic and Statistical Manual of Mental Disorders, 5$^{th}$ edition (DSM 5) (17). Although DSM is more commonly used in the Western countries and for research purposes, ICD-10 criteria are in our environment officially accepted for diagnosis (15).

Criteria mentioned by DSM 5 include the presence of two or more characteristic symptoms delusional ideas, hallucinations, unorganized speech, catatonia or negative symptoms (avolition, desocialization, autism) that persist for most of the time during one month with uninterrupted signs of normal functioning during at least 6 months (18). It is of utmost importance, besides talking to the patient, to talk to other family members or people close to the patient in order to establish the diagnosis. A valid diagnosis should also exclude any other primary mood disorder, schizoaffective disorder, intoxication or withdrawal syndrome, or any other condition (15). Unfortunately, the time that passes from the onset of the first symptoms of schizophrenia till the arrival to the doctor for a treatment is often too long and lasts for 3-5 years, or longer. The resistance of positive and/or negative symptoms in schizophrenia means resistance to psychopharmaceuticals or persistence of symptoms in patients regardless of

therapy. Even 40-70% of patients with therapeutic-resistant schizophrenia suffer from symptoms despite adequate clozapine therapy (19). In this case, ECT is used as "last-resort" therapy. States in schizophrenia that are most frequently treated with ECT are antipsychotic therapy resistance, affective symptoms, catatonia, neuroleptic malignant syndrome (NMS). Of these, the most successful treatment is the one of catatonia, and then positive symptoms such as paranoid delusional ideas and affective symptoms (20).

Depression is today the most common indication for ECT. The word depression is derived from the Latin word *deprimere*, which means to depress, suppress, press (21). This is a mood disorder in which the patient is pervaded by the feeling of sadness, s/he loses any will for the activities, even for those that once brought pleasure. Except for these two symptoms, there are some others, such as sleep disorders, changes in appetite and weight, hyposexuality, social isolation, lack of energy, poor concentration, and psychomotor problems, sense of worthlessness and guilt, and suicidality (22).
It is important to distinguish between a major depressive disorder (MDD), a bipolar disorder and a mood disorder caused by some other medical diagnosis (e.g. tumor). It is also important to differentiate a major depressive disorder from a major depressive episode (MDE). The major depressive disorder is chronic disease characterized by relapses, and the depressive episode is when depression occurs for the first time. Depressive episodes vary in intensity from mild, moderate, to severe depressive episodes with or without psychotic symptoms, and the symptoms should last at least two weeks, every day, almost all day (21). To diagnose a new depressive episode or a major depressive disorder, there must be a period of at least 2 months without depressive symptoms, before a new depressive episode emerges (21). Just as with schizophrenia, one of two classifications can be used: ICD-10 or DSM-5.
In recent years, depression is on the rise. It is believed that by 2020 depression will be the second most common place in the world immediately after cardiovascular diseases (21). Depression is almost twice as likely in women as in men (2:1), regardless of race, ethnicity or socioeconomic status (21).

Antidepressants, which are widely used today, in as many as 30-40% of patients who take them regularly, they are ineffective (22). In such patients, the ECT has been proved as an effective "antidepressant". The percentage of success, i.e. effectiveness of ECT in clinical trials on depression is as high as 70-90% (23).

Bipolar affective disorder (BAD) is a mood disorder, with characteristic switching between depressive, manic and hypomanic episodes. The manic episode of BAD is characterized by an elevated, irritable mood in combination with three or more of following symptoms: reduced need for sleep (insomnia), grandiosity or excessive self-confidence, fast and hurried speech, lack of focus, problematic behavior, a stream of thoughts and ideas, participation in risky activities (24). Hypomania is similar to mania, but it's not psychotic to the point that it creates functional problems for the patient that would require hospitalization. In order to diagnose a depressive episode, just like for depression, the symptoms must be present for at least 2 weeks. There is also a mixed episode that has elements of manic and depressive episodes, almost every day for a week.

Bipolar affective disorders can be divided into bipolar disorder I, II, cyclothymic disorder (cyclothymia). Bipolar disorder I is defined by a manic episode that lasts for at least seven days or manic symptoms that are so serious that a person needs urgent hospitalization and depressive episodes that last for at least two weeks. Bipolar disorder II is characterized by depressive and hypomanic episodes. Cyclothymia is a characteristic alteration of many hypomanic and depressive symptoms over a period of two years, but the symptoms do not meet the criteria for diagnosing hypomanic or depressive episodes (25). Depressive symptoms are relatively easy to recognize, and the person herself/himself will notice that they are not feeling as good as they normally do. The problem arises when a person needs to be convinced that his or her manic episodes are not part of normal behavior.
For diagnosis, we use one of the two standard classifications: ICD-10 or DSM 5. Bipolar affective disorder can range from 0.3 to 1.5% of the total adult population, and appear in the same ratio in women and men (26). For the first time, they typically occur during adolescence up to the early 20s in the form of depressive episodes (27).
Bipolar disorders are commonly treated with so-called mood stabilizers. In addition, they can be treated with typical and atypical antipsychotics, but also with ECT (6). Even though, ECT has proved its superiority over lithium – the most well-known mood stabilizer (28) through many research, the ECT will be seen as the first line treatment only in the case of psychotic mania (29).

Suicidality is the next significant indication for treatment with ECT. The world suicide is a compilation of two Latin words: *sui* and *occidere* what in literal translation means to kill yourself (30). Silverman et al. classify suicidal behavior as a suicide threat, a suicide plan, self-injury, suicide attempt, suicide, indefinite conduct related to suicide (30). Psychiatric

disorders that carry 10-15% higher risk of suicide than other disorders and psychiatric diagnoses are BAD, alcoholism and depression, followed by schizophrenia, personality disorders and other addictions (31). The suicide rate in bipolar disorders is 164/100 000 persons per year (32) and in schizophrenic patients 579/100 000 people per year (33). According to Mayo Clinic survey, 2-9% of people diagnosed with depression during their life will commit suicide, that is, they will successfully take away their life (34). Voracek and Lobil found that suicidal behavior is inherited in 30-55% of cases and is very likely independent of psychiatric disorders (35).
Five of the most common forms of suicidality determined by the dimensions of the disease are: psychotic (as a result of frenzy and hallucination), depressive (as a result of feeling of hopelessness), disorganized (disorganized functionality, confusion without conscious desire for suicide), alienation (associated with lack of appropriate social support as a result of withdrawal from social life), and ultimately reactive suicidality (as a reaction to stressful events, family conflicts) (30).
According to the World Health Organization (WHO), about 800 000 people commit suicide each year, which would mean roughly one life is lost every 40 seconds (36). Even more alarming is the fact that suicide is the second leading cause of death in people aged 15 to 29 years. Suicide, which appears as a symptom of mental illness, is treated conservatively with antidepressants in combination with antipsychotics, but as well with ECT and psychotherapeutic methods. Suicidality as an indication for ECT may be acute suicidality or chronic continuous suicidality which does not respond to conventional methods of treatment.

Neuroleptic malignant syndrome (NMS) is life-threatening and emergency condition caused by psychopharmaceutical drugs. This potentially lethal complication is recognizable by hypothermia muscular rigidity, changed consciousness state, and autonomic nervous system dysfunction (37). The muscle rigidity, that is, the heat that the muscle produces is such state could explain hyperthermia, which can lead to dehydration and electrolyte disbalance, putting the patient at increased risk for infection (38). Laboratory findings, such as elevated serum creatine phosphokinase (CPK), could also be explained by the rigidity of the muscles and their self-destruction, which leads to myoglobinuria and acute kidney failure (38). Other laboratory findings are leukocytosis and elevated liver enzymes (39). The frequency or neuroleptic malignant syndrome in patients who are treated with antipsychotics of the first generation, selective serotonin reuptake inhibitors (SSRI), monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCA) was estimated to be 0.5% (39). Frequency is

higher in young men who are malnourished and dehydrated, have Parkinson's disease or parenterally receive high doses of neuroleptics over a short period of time (40). Some papers confirm that the risk for NMS is higher in patients received ECT (41). It is unknown what exactly causes NMS in some people, and in others, it does not. It is thought that NMS is caused by blockade of hypothalamic and striatal dopamine receptors, as they also act on thermoregulation and muscular spasm (39). Once a patient is diagnosed with NMS, antipsychotics are immediately discontinued and bromocriptine is administered, and sometimes the ECT is used. The temperature, just like the electrolytes, is tried to be withheld within the normal limits (39). It has also been confirmed that there is no certain type of neuroleptic that has greater or lesser potential for NMS, however, it is generally considered that typical antipsychotics have a greater risk (38).

## HYPOTHESIS

1) Indications for ECT in the treatment of major mental disorders, compared to traditional indications, have been extended to suicidality, catatonic state, MNS, schizophrenia, depression, and therapeutic resistance in mental disturbances.
2) There are sex and age differences between patients treated with ECT in regard to the diagnosis of mental illness and the indication for the ECT.

## OBJECTIVES

The aim of the study is to examine the general and specific features of patients treated with ECT in the period from 2010 till 2017 at the Clinic for Psychiatry, Clinical Hospital Center Zagreb.

General demographic characteristics will determine the sex and age distribution of the patient, as well as other characteristics related to work, education, family and social status and heredity.

The frequency of mental diseases diagnoses in patients treated with ECT, type of early therapy attempts, suicidal attempts, psychoactive substance abuse and the number of psychiatric hospitalizations to date will be investigated. The age when the first psychiatric treatment begins and the age of the first application of the ECT will be investigated. Indications for the application of the ECT will be analyzed in 6 specific groups of indications: suicidality, therapeutic resistance to schizophrenia with positive symptoms and schizophrenia with negative symptoms, therapeutic resistance to all diagnoses, catatonia, and NMS.

The number of applications, side effects, and termination of therapy will be analyzed and outcome in the form of re-hospitalization of patients within the first year after the ECT.

## METHODS

This study is a retrospective analysis of the medical documentation of the patients treated with ECT from 2009 till 2017 at the Clinic for Psychiatry at the Clinical Hospital Center Zagreb. In this period 213 patients have been treated with ECT. All patients had a history of previous psychiatric treatment, as well as recorded earlier multiple-course therapeutic trials using conventional treatment methods. Patients underwent standard clinical protocol for ECT which includes hospitalization. The protocol also includes psychiatric evaluation, diagnosis and confirmation of ECT indication, general laboratory findings, EEG, CT of the brain, internal medicine specialist, and anesthesiologist check-up, and exclusion of contraindications for the electroconvulsive therapy. Psychiatric diagnoses were based on ICD-10 (16).

Patients are referred to ECT by the department psychiatrist, psychiatrist from another institution in the city, region or even state. All patients had to sign an informed consent for the ECT, and the Ethics Committee of Clinical Hospital Center Zagreb had to approve every single case in order for the therapy to be performed. A bitemporal ECT was used, and patients were situated in the intensive care unit during the ECT treatment. The ECT was performed 3 times a week, and during the applications, the patients received their usual or customized pharmacological therapy unhindered. The ECT is being performed as a medical intervention in short-term anesthesia by a team of a psychiatrist, an anesthesiologist, an anesthesiologist technician, a psychiatric medical technician and nursing staff. Premedication was atropine, 0.5 mg subcutaneously, 30 minutes before ECT, with the aim of preventing increased salivation and decreased heart rate during stimulation. Anesthetized intravenous medications that relieve the muscles and cause short-term deep sleep (most often propofol and lysthenone in dilution according to anesthesiologist recommendation), with vital signs monitoring. The ECT is applied by a psychiatrist for a few seconds (2-5 seconds) so that the electrode of the apparatus touches the temple area, both sides. The whole procedure, including anesthesia induction and awakening, lasts 5 to 10 minutes.

All data on hospitalization, ECT and the patients themselves were obtained from the patients' history in its written and/or digital form. They were analyzed according to the age, sex, number of previous hospitalizations, previous therapies, diagnosis, leading diagnosis, number of ECT applications and outcome. Statistical analyses were carried out by the SPSS computer software (19.0 version for Windows). The methods used for descriptive statistics are frequency methods, percentages, arithmetic mean, standard deviation, minimum and maximum value. Interferential statistical analyses included a chi-square test, a t-test for independent samples and a one-way variance analysis (ANOVA) with the associated post hoc Scheffe test. The level of statistical significance was set at 5%, $p = 0.05$.

## RESULTS

Table 1. Sociodemographic features of the sample

| | | Frequency | Percentage | Valid Percentage | Cumulative Percentage |
|---|---|---|---|---|---|
| Sex | Men | 105 | 49.3 | 49.3 | 49.3 |
| | Women | 108 | 50.7 | 50.7 | 100.0 |
| Education | Primary school | 19 | 8.9 | 8.9 | 8.9 |
| | Secondary school | 148 | 69.5 | 69.5 | 78.4 |
| | Higher education | 46 | 21.6 | 21.6 | 100.0 |
| Employment status | Missing | 1 | .5 | .5 | .5 |
| | Unemployed | 95 | 44.6 | 44.6 | 45.1 |
| | Employed | 54 | 25.4 | 25.4 | 70.4 |
| | Retired | 48 | 22.5 | 22.5 | 93.0 |
| | Educating | 15 | 7.0 | 7.0 | 100.0 |
| Marital status | Single | 112 | 52.6 | 52.6 | 52.6 |
| | Married | 92 | 43.2 | 43.2 | 95.8 |
| | Divorced/Widowed | 9 | 4.2 | 4.2 | 100.0 |
| Parenthood | None | 120 | 56.3 | 56.6 | 56.6 |
| | With kids | 92 | 43.2 | 43.4 | 100.0 |
| | In total | 212 | 99.5 | 100.0 | |
| | Missing | 1 | .5 | | |
| Heredity | None | 66 | 31.0 | 31.0 | 31.0 |
| | Mother | 23 | 10.8 | 10.8 | 41.8 |
| | Father | 24 | 11.3 | 11.3 | 53.1 |
| | Brother/Sister | 8 | 3.8 | 3.8 | 56.8 |
| | Other cousins | 40 | 18.8 | 18.8 | 75.6 |
| | Unknown | 52 | 24.4 | 24.4 | 100.0 |
| In total | | 213 | 100.0 | 100.0 | |

Out of 213 hospitalized psychiatric patients, there was approximately the same number of women (N = 108) and men (N = 105), of which most of them finished at least secondary school (N = 148). The majority of them were either unemployed (N = 95) or retired (N = 48), in total 143 patients without a job. Considering marital status 112 patients were single, 9 divorced and 92 married, while 43.2% has children. Heredity is positive in 44.7% of the patients.

Table 2. Analysis of psychiatric treatment

| | | Frequency | Percentage | Valid Percentage | Cumulative Percentage |
|---|---|---|---|---|---|
| Diagnoses | Schizophrenia | 120 | 56.3 | 56.3 | 56.3 |
| | Delusional disorder | 3 | 1.4 | 1.4 | 57.7 |
| | Acute psychotic episode | 4 | 1.9 | 1.9 | 59.6 |
| | Shizoaffective | 32 | 15.0 | 15.0 | 74.6 |
| | Non-organic psychosis | 1 | .5 | .5 | 75.1 |
| | BAD | 25 | 11.7 | 11.7 | 86.9 |
| | Depression | 2 | .9 | .9 | 87.8 |
| | Recurrent depression | 26 | 12.2 | 12.2 | 100.0 |
| Clozapine | Yes | 110 | 51.6 | 51.6 | 51.6 |
| | No | 103 | 48.4 | 48.4 | 100.0 |
| | In total | 213 | 100.0 | 100.0 | |
| Suicide attempt | No | 171 | 80.3 | 80.3 | 80.3 |
| | One attempt | 24 | 11.3 | 11.3 | 91.5 |
| | More attempts | 18 | 8.5 | 8.5 | 100.0 |
| Rehospitalization after ECT | No | 164 | 77.0 | 77.0 | 77.0 |
| | Yes | 49 | 23.0 | 23.0 | 100.0 |
| In total | | 213 | 100.0 | 100.0 | |

The average number of hospitalizations before ECT was 4.7 (sd = 4.65143, range 0-24 times). The average age of the first psychiatric treatment was 29.3 years (sd = 12.15233, range 11-66 years). The average age of the first treatment with ECT was 39.1 (sd = 12.942, range 18-77 years). Before the ECT all patients were treated with combined pharmacotherapy, most often antipsychotics (100%), antidepressants (39%), mood stabilizers (35%) and anxiolytics (92%).

Table 3. Analysis of ECT features

Average number of ECT applications was 9.5 (sd = 3.54962, range 1-18) in 213 patients.

| | | Frequency | Percentage | Valid Percentage | Cumulative Percentage |
|---|---|---|---|---|---|
| Indications for ECT | Suicidality | 24 | 11.3 | 11.3 | 11.3 |
| | Resistance to therapy | 51 | 23.9 | 23.9 | 35.2 |
| | Therapy resistant schizophrenia with positive symptoms | 94 | 44.1 | 44.1 | 79.3 |
| | Therapy resistant schizophrenia with negative symptoms | 25 | 11.7 | 11.7 | 91.1 |
| | NMS | 4 | 1.9 | 1.9 | 93.0 |
| | Catatonia | 15 | 7.0 | 7.0 | 100.0 |
| Disrupting ECT | No | 27 | 12.7 | 12.7 | 12.7 |
| | Yes | 186 | 87.3 | 87.3 | 100.0 |
| ECT side effects | No | 198 | 93.0 | 93.0 | 93.0 |
| | Somnolence | 11 | 5.2 | 5.2 | 98.1 |
| | Restlesness | 1 | .5 | .5 | 98.6 |
| | Cognitive s.e. | 3 | 1.4 | 1.4 | 100.0 |
| In total | | 213 | 100.0 | 100.0 | |

Table 4. Comparison according to age and sex

Women and men differ considerably (according to the t-test) considering the age of the first ECT application: women are older than men.

| | Sex | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Age of ECT application | Male | 105 | 35.3558 | 12.05160 | 1.18176 |
| | Female | 108 | 42.7736 | 12.78413 | 1.24170 |

| | | 95% Confidence Interval od the Difference | | |
|---|---|---|---|---|
| | | T | Df | Sig. (2-tailed) |
| Age of ECT app. | Equal variances assumed | -4.325 | 208 | .000 |
| | Equal variances not assumed | -4.327 | 207.671 | .000 |

Table 5. Comparison according to sex and prevalence of individual psychiatric diagnoses

Women and men statistically differ significantly according to the prevalence of individual diagnoses (based on the chi-square test): among men, there is a significantly higher number of those diagnosed with schizophrenia, while among women there are more depression and schizoaffective disorders diagnosed. Women and men don't differ when it comes to diagnosis of BAD.

| **sex * diagnosis Cross tabulation** | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Diagnosis | | | | In total |
| | | | Schizophrenia | SAD | BAD | Depression | |
| Sex | Male | Count | 76 | 10 | 12 | 7 | 105 |
| | | % within the gender | 72.4% | 9.5% | 11.4% | 6.7% | 100.0% |
| | | % of men diagnosed with | 59.4% | 31.3% | 48.0% | 25.0% | 49.3% |
| | | % out of total | 35.7% | 4.7% | 5.6% | 3.3% | 49.3% |
| | Female | Count | 52 | 22 | 13 | 21 | 108 |
| | | % within the gender | 48.1% | 20.4% | 12.0% | 19.4% | 100.0% |
| | | % of women diagnosed with | 40.6% | 68.8% | 52.0% | 75.0% | 50.7% |
| | | % out of total | 24.4% | 10.3% | 6.1% | 9.9% | 50.7% |
| In total | | Count | 128 | 32 | 25 | 28 | 213 |
| | | % within the gender | 60.1% | 15.0% | 11.7% | 13.1% | 100.0% |
| | | % of diagnosed patients | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % out of total | 60.1% | 15.0% | 11.7% | 13.1% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 16.001a | 3 | .001 |
| Likelihood Ratio | 16.462 | 3 | .001 |
| Linear-by-Linear Association | 11.258 | 1 | .001 |
| N of Valid Cases | 213 | | |

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 12.32.

Table 6. Comparison according to sex and the indication for ECT

1 = therapy resistant mood disorder; 2 = therapy resistant schizophrenia with positive symptoms; 3 = therapy resistant schizophrenia with negative symptoms

| **indication2 * sex Cross tabulation** | | | | | |
|---|---|---|---|---|---|
| | | | Sex | | In total |
| | | | Male | Female | |
| Indication | 1 | Count | 19 | 32 | 51 |
| | | % within the indications | 37.3% | 62.7% | 100.0% |
| | | % within the gender | 23.2% | 36.4% | 30.0% |
| | | % out of total | 11.2% | 18.8% | 30.0% |
| | 2 | Count | 54 | 40 | 94 |
| | | % within the indications | 57.4% | 42.6% | 100.0% |
| | | % within the gender | 65.9% | 45.5% | 55.3% |
| | | % out of total | 31.8% | 23.5% | 55.3% |
| | 3 | Count | 9 | 16 | 25 |
| | | % within the indications | 36.0% | 64.0% | 100.0% |
| | | % within the gender | 11.0% | 18.2% | 14.7% |
| | | % out of total | 5.3% | 9.4% | 14.7% |
| In total | | Count | 82 | 88 | 170 |
| | | % within the indications | 48.2% | 51.8% | 100.0% |
| | | % within the gender | 100.0% | 100.0% | 100.0% |
| | | % out of total | 48.2% | 51.8% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 7.156[a] | 2 | .028 |
| Likelihood Ratio | 7.218 | 2 | .027 |
| Linear-by-Linear Association | .357 | 1 | .550 |
| N of Valid Cases | 170 | | |

Indications differ significantly according to gender: in groups of indications of therapy-resistant mood disorders and therapy-resistant schizophrenia with negative symptoms are more women, while in the group of indications of therapy-resistant schizophrenia with positive symptoms more men.

Table 7. Age and indication for ECT

1 = therapy resistant mood disorder; 2 = therapy resistant schizophrenia with positive symptoms; 3 = therapy resistant schizophrenia with negative symptoms

| Table. Comparison according to the age and indication for ECT | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | |
| | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | Minimum | Maksimum |
| AGE ECT | | | | | Lower Bound | Upper Bound | | |
| 1 | 49 | 48.1837 | 12.48778 | 1.78397 | 44.5968 | 51.7706 | 18.00 | 77.00 |
| 2 | 93 | 33.6667 | 10.43961 | 1.08254 | 31.5167 | 35.8167 | 18.00 | 64.00 |
| 3 | 25 | 41.8800 | 13.16979 | 2.63396 | 36.4438 | 47.3162 | 20.00 | 64.00 |
| In total | 167 | 39.1557 | 13.13873 | 1.01671 | 37.1483 | 41.1630 | 18.00 | 77.00 |

Table 8. ANOVA test

| AGE ECT | Sum od Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 6981.298 | 2 | 3490.649 | 26.412 | .000 |
| Within Groups | 21674.654 | 164 | 132.163 | | |
| In total | 28655.952 | 166 | | | |

Table 9. Differences between indications according to age

1 = therapy resistant mood disorder; 2 = therapy resistant schizophrenia with positive symptoms; 3 = therapy resistant schizophrenia with negative symptoms

| (I) Indication | (J) Indication | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| 1 | 2 | 14.51701* | 2.02936 | .000 | 9.5039 | 19.5301 |
| | 3 | 6.30367 | 2.82554 | .086 | -.6762 | 13.2835 |
| 2 | 1 | -14.51701* | 2.02936 | .000 | -19.5301 | -9.5039 |
| | 3 | -8.21333* | 2.58990 | .008 | -14.6111 | -1.8156 |
| 3 | 1 | -6.30367 | 2.82554 | .086 | -13.2835 | .6762 |
| | 2 | 8.21333* | 2.58990 | .008 | 1.8156 | 14.6111 |
| *. Statistical significance at 0.05 level. | | | | | | |

According to variance analysis (ANOVA), significant differences were found between three age-related indications: the post-hoc Scheffe test shows that indications 1 and 2 differ significantly (patients with mood disorders are significantly older than patients with schizophrenia with positive symptoms), and indications 2 and 3 (patients with schizophrenia with negative symptoms are significantly older than patients with schizophrenia with positive symptoms) (Table 7 and 8).

## DISCUSSION

In the period from January 1st, 2010 until March 1st, 2017 in the Department of Psychiatry of the Clinical Hospital Center Zagreb there were 213 patients of both sexes (m = 105, w = 108) who received ECT. All patients were hospitalized during the therapy. The indication for the treatment with the ECT was set up by a competent psychiatrist. Each patient signed a special informed consent for the treatment with the ECT and then received the approval of the hospital Ethics Committee. The most common indication for the treatment with the ECT was therapy resistance and considering diagnostic categories, schizophrenia and mood disorders.

### Analysis of demographic characteristics and heredity of patients on ECT

The average age of the patients in the study was 39 years, with male patients being considerably younger than female patients on ECT. Many studies find the significantly earlier age of the first ECT application in the age group of 20-29 years, which differs from the average age of our examined group (42, 43). However, in American Centers, the average age of patients getting the ECT is older (44). The ECT in the treatment of psychiatric disorders is considered equally effective in all age groups (45).
In our examined group there was an almost equal number of female and male patients who received the ECT. Some studies find a higher incidence of female patients on the ECT (46, 47).

Most patients have a secondary school education (N = 148), they are not working (unemployed = 95, retired = 48), and approximately every other has not married (N = 112) and has no children (N = 120). The first episodes of all major psychiatric disorders (psychosis, depression, BAD) often occur in adolescence and early adulthood and have an adverse effect on schooling, school, and academic success, normal psychological development, social and emotional ties, employment and self-reliance (1). The clinical significance and intensity of mental illness and the failure of conventional therapeutic methods that later result in treatment with ECT may also be the reason for the inability to set up a family and to hire or retire. Heredity is positive in 44.4% of patients, which is higher than expected in the general population. According to previous research, the expected heredity for schizophrenia is 6-18%, for depression and BAD is higher. A higher percentage of heredity in a group of patients receiving ECT can be interpreted by the increased clinical intensity and/or disability caused by mental disorder. The anticipatory theory of inheritance of schizophrenia

presupposes the early occurrence of diseases and severe forms of disease in the next vertical generation (1). In ¼ of patients, there is no data on heredity, which does not mean the absence of heredity, so the percentage of heredity is probably even higher.

The mean age of the first psychiatric treatment (M = 29.3) is, as expected, earlier than the age of the first received ECT (M = 39.1), and the wide range is visible in both cases. The youngest patient that received ECT application was 18 years old and the oldest was 77 years of age. The average length of psychiatric treatment is indicative before deciding to treat with ECT. On average, it passes 10 years from the first psychiatric treatment to the first application of ECT, indicating a certain therapeutic inertia, a physician's inability, and prejudices towards the treatment with ECT by patients, families, and specialists as well. Although there is no information on Duration of untreated psychosis (DUP) before the first psychiatric treatment, the average age of the first treatment is 29 years, which indicates late recognition of the disease and consequently late treatment. Late recognition and late treatment of the psychiatric illness, especially psychosis, is connected with unfavourable outcome of the treatment, decreased quality of life, and probably with progression of psychiatric disease with development of the clinical picture, dysfunctionality and disability of the patient, as well as unfavourable effect on the biology of the brain (1). The earlier treatment is connected with the better therapeutic response, which decreases the risk of therapeutic resistance and treatment failure, and in that way, we avoid invasive treatments, such as ECT. The average number of psychiatric hospitalizations prior to the ECT therapy is 4, with the maximum being 24. The phenomenon of frequent psychiatric hospitalizations (revolving door) is connected with low compliance, avoidance to take the prescribed therapy, unfavorable social and familial status and with less intensive symptoms. Therapeutic resistance could be the factor responsible for frequent psychiatric hospitalizations. For the patients in this research, we confirmed the failure of conventional forms of treatment.

**Analysis of diagnoses of psychiatric patients on ECT**

Patients who were treated with ECT, most commonly had following diagnoses: schizophrenia and psychoses (N = 160), depression (N = 28) and BAD (N = 25). In this sample, there is no other diagnostic category which, according to the literature could have gained benefits from ECT (e.g. dementia, PTSD, obsessive-compulsive disorders etc.), and this designates the strict frame of indications seen in clinical praxis. This proves that praxis in Croatia is very similar to the one in Hungary, Czech Republic, Estonia, Lithuania, where schizophrenia is the main diagnosis that is treated with ECT, whereas, for Poland, Slovakia, Bulgaria, Ukraine, and Serbia the main diagnoses are affective disorders (48).

Earlier suicide attempts are noted in 18% of patients, and suicidality as an indication for ECT was noticed in 11% of patients. Differences exist due to suicidality being transdiagnostic and dynamic psychological phenomenon; it is rarely acute indication for ECT. Suicidality, as an indication for ECT, is observed as continuity of suicidal ideas and compulsions, with or without attempts, and of a chronic character. No patients were treated with ECT because of acute suicidality or the first episode of suicidality. The frequency of suicidality in this sample is in correlation with expected frequency of suicidality, considering the diagnoses of schizophrenia, depression and BAD.

**Analysis of treatment before ECT**

All the patients were treated with combined pharmacotherapy in many therapeutic attempts before ECT. Most commonly these were antipsychotics (100%), anxiolytics (92%), antidepressants (39%), and mood stabilizers (35%). This was also a requirement to define therapeutic resistance and approval from the Ethics Committee. Half of the patients were already treated with clozapine – antipsychotics reserved for resistant psychosis and suicidality. Therefore, we can consider ECT a “last-resort” therapy for the therapeutic resistant states (49).

**Analysis of indications for ECT treatment**

Diagnosis of psychiatric disease per se is not an indication for ECT treatment. Indications for applications of ECT are determined individually for each patient. Most commonly it depends on the success or failure of the treatment and the endurance of the disease symptoms or the

existence of risk states such as suicidality or aggressiveness, catatonia, and NMS. In this study, we investigated specific indications for referral of patients to treatment with ECT, relative to the primary diagnosis of mental illness.

For the period of 7 years, the most common indication for treatment with ECT was the evaluation of therapeutic resistance, meaning lack of therapeutic response to conventional treatment methods, mainly combined pharmacotherapy (N = 79.7%). Traditionally, primary indications for ECT suicide and catatonia, and NMS are significantly less represented. If a strict indicative framework of primary indications was used to determine indications (suicidality and catatonia) only 39 patients would receive ECT therapy, as opposed to 213 patients.

Studies show significant differences in indications for ECT in other clinical centers, Generally, in developed countries, primary ECT indications are mood disorders, i.e. depression (50,51). In Asian countries, common indications are schizophrenia and psychosis (52). In one Indian study from 2011, the most common indications for ECT in schizophrenia patients were augmentation of pharmacotherapy, followed by therapeutic response urgency and treatment resistance, which is only partly consistent with findings of this study where treatment resistance was the first indication (53). The results that were the most similar to the results of this study are the ones from Hungarian practice, where through surveys they concluded that psychiatrists most frequently recommended ECT for antipsychotic and antidepressant-resistant patients (54). This study shows a higher incidence of treatment with ECT due to therapeutic resistance, while treatment of primary indications, suicidality, and catatonia is less represented in this sample. According to literature, the pattern of ECT frequency is somewhat higher on the side of mood disorders, i.e. depression, relative to schizophrenia and psychosis, as opposed to this sample having a reverse indicative pattern. With regard to more than thirty years of experience with ECT at the Psychiatric Clinic, this trend indicates the probable effect of clinical experience and practice in treating primarily therapeutic resistance in schizophrenia, and then in other indications, while suicide and catatonia are less represented (55). A small number of NMS (4 patients) is probably due to a greater prescription of atypical antipsychotics in modern psychiatry and the frequency of treatment with clozapine.

**Indications for ECT with regard to age and sex of the patient**

The trend of referral of patients to therapy at the Psychiatric Clinic is significantly different in relation to the gender of the patient relative to the indications. Male patients getting treated with ECT are more likely to have the diagnosis of schizophrenia than female patients. Women referred to ECT more often suffer from depression and schizo-affective disorders. For the diagnosis of BAD, there are no differences between sexes.

This corresponds to the previous findings that in Western countries majority ECT treated are older women with depression on contrary to younger men with schizophrenia in Asian countries (56). However, even in Asia, there are exceptions. In Japan, Hong Kong, Pakistan and Saudi Arabia, female sex and depression predominance were also observed, except for the younger age (56). In this study, women who have been referred to the ECT at the same time, apart from the diagnosis, are also different at age – they are older than male patients receiving ECT. This trend suggests a longer waiting period to indicate the treatment for ECT in women, which can be explained by the gender differences in the course and outcome of mental illness. Sexual differences in mental illness are related to differences in bio-psycho-social changes – in women, psychoses occur at a later age, effectively more adequate, they use their social, working and family potentials better, partly because of a different social pattern of relationships with women in the community. Hormonal differences also have an effect on e.g. behavior, so in men, aggressive behavior that is in conjunction with productive symptoms becomes a significant risk to the environment. It is generally considered that female sex has a better treatment outcome than male in schizophrenia. Although women are more likely to suffer from depression, men (probably depressed) are more likely to commit suicide, again proving sexual differences in mood disorders and suicidality. Swedish study proved that among severely depressed inpatients that received ECT (38%), the proportion treated with ECT was higher among women (1105/2771; 40%) than men (661/1940; 34%) (56). The other studies also point to a higher proportion of women on ECT then men (57), whereas, in this study, the number of males and females treated with ECT is almost the same (women = 108, men = 105). It seems that Croatia did not completely follow the shift in Western world practice and the increasing use of ECT among women found both in USA and Australia (56). This study shows significant age-diagnostic differences in the patient's group: on ECT therapy, younger patients have more resistant, predominantly susceptible symptoms of schizophrenia, and older patients are more often suffering from mood disorders and schizophrenia with negative symptoms. Considering the age issue, this study corresponds with

findings in western countries (Australia, New Zealand, USA, Europe), where the median age of patient receiving ECT was above middle age (56).
In this research there are differences in gender with regard to indications for ECT: male patients are more likely to have a dominant positive picture of schizophrenia, and female schizophrenia with negative symptoms and mood disorders – depression and BAD. Differences in sex are also manifested by the indication for ECT. Schizophrenia with positive symptoms, resistant to pharmacotherapeutic treatment attempts is more frequently treated and at the earlier age by ECT in men. This could be explained by the need for a better control of positive symptoms (hostility, delusions – paranoia, hallucinations, disorganized behavior, and thinking, etc.). In women, the development of the disease takes a longer time, and schizophrenia with negative symptoms is somewhat calmer, however not less serious because it leads to significant dysfunctionality (decline in volition, reduction in affect, withdrawal, avoidance of daily activities and social contact, etc.). BAD resistant to therapy is most common indication due to the mixed clinical picture, fast-cycling form and psychotic intensity of mania and depression. Other studies show mixed results as well, in regards to the relation between sex and indication for ECT, and more frequent indication for women are affective disorders (52).

**Number of ECT applications and side effects**

On average, patients received 9 ECT applications, ranging from 1 to 18 applications. The anticipated number of applications in this treatment method ranges from 12 to 15, and the number of applications with minimal clinical effect is 6. A lower number of applications could imply side effects in older patients or inefficiency estimates. In 12% of patients, the therapy was discontinued and 7% had side effects (confusion, forgetfulness, etc.). In general, side effects of ECT are considered rare and of a transient character, and most commonly described are acute cognitive disturbances associated with effects of anesthesia (58). No serious and persistent side effects of treatment have been reported in this study. This is consistent with the overall worldwide experience where the report of side effects, adverse events, and the mortality rate is sparse (56).

**Outcome of ECT**

The effect of ECT was assessed by analyzing the frequency or re-hospitalization of patients within a year (59). Within a year after ECT, 23% of the patients were re-hospitalized, and there was no significant difference in relation to the three different indications. Indications for re-hospitalization may be numerous, ranging from clinical deterioration to adverse socioeconomic and family circumstances and relationships in which patient lives. It can be said that in 2/3 patients the therapy with ECT has sufficiently calmed the symptoms of mental illness, which made it possible to continue the outpatient treatment of the patient for the patient to return to his community and improve his quality of life. The best therapy is combined therapy, and it has already been proven that reduction in the re-hospitalization rate in ECT group is more pronounced among those treated with clozapine or a medium-high average daily dose of antipsychotics (60). The goal of psychiatric treatment is to treat out-of-hospital patients in outpatient, outpatient or community settings, enabling better rehabilitation of patients in their family and community.

## CONCLUSIONS

Therapeutic resistance gains increasing significance as an indication for the treatment with ECT, next to primary indications: suicidality, catatonia, neuroleptic malignant syndrome. ECT is becoming more commonly used for therapeutic resistance to conventional treatment methods in schizophrenia and mood disorders. Apart from differences in the area of relevance for the diagnosis of mental illness, referral of patients to ECT may vary according to age, sex, and features that dominate the clinical picture of schizophrenia (positive or negative symptoms), and it also depends on clinical praxis and experience of the centers that provide ECT as a therapy. The best results in treating therapy resistance are expected in combined treatment, pharmacotherapy with ECT. Research on the application of ECT as a treatment for mental illnesses will provide a better understanding, enable targeted and timely set indications, and it will neutralize controversies associated with this treatment method.

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## REFERENCES


1. Jakovljević M, Biološka terapija u psihijatriji. In: Begić D, Jukić V, Medved V., ed. Psihijatrija. Zagreb: Medicinska Naklada, 2015;363.
2. Fink M. Meduna and the origins of convulsive therapy. Am. J. Psychiatry 1984;141:1034-1041.
3. Dunne RA, McLoughlin DM. Electroconvulsive therapy and therapeutic neuromodulation. In: Wright P, Stern J, Phelan M., ed. Core Psychiatry, 3. izadnje. Philadelphia: Saunders, 2012;617-627.
4. Sabbatini R. The history of shock therapy in psychiatry. Available at: http://www.cerebromente.org.br/n04/historia/shock_i.htm
5. Taylar CE. Electroconvulsive therapy. Can Fam Physician 1984;30:391-394.
6. Baghai TC, Möller HJ. Electroconvulsive therapy and its different indications. Dialogues Clin Neurosci. 2008;10(1):105-117.
7. Rudorfer MV, Herny ME, Sackeim HA. Electroconvulsive Therapy (ch. 92). In: Tasman A, Kay J, Lieberman JA, First MB, Riba MB., ed. Psychiatry, 4th edition
8. Mayo C, Kaye AD, Conrad E, Blauch A, Frost E. Update on anesthesia considerations for electroconvulsive therapy. Middle East J Anesthesiol. 2010;20:493-498.
9. Sackeim HA. Autobiographical memory and electroconvulsive therapy: do not throw out the baby. J ECT 2014;30:177-186.
10. Sackeim HA, Prudic J, Nobler MS, Fitzsimons L, Lisanby SH, Payne N et al. Effects of pulse width and electrode placement on the efficacy and cognitive side effects of electroconvulsive therapy. Brain Simulation 2008;1:71-83.
11. Sobin C, Sackeim HA, Prudic J, Devanand DP, Moody BJ, McElhiney MC. Predictors of retrograde amnesia following ECT. Am J Psychiatry 1995;152:995-1001.
12. Santos Jr. A, Oliveira MC, dos Santos Andrade T, Ramos de Freitas R, Muller Banzato CE, Cruz Soares de Azevedo R, Botega NJ. Twenty year of electroconvulsive therapy in a psychiatric unit at the university general hospital. Trends in Psychiatry and Psychotherapy 2013;35(3):229-233.
13. Caroff SN. The neuroleptic malignant syndrome. J Clin Psychiatry 1980;41:79-83.
14. Iancu J, Pick N, Seener-Lorsh O, Dannon P. Patients with schizophrenia or schizoaffective disorder who receive multiple electroconvulsive therapy sessions: characteristics indications and results. Neuropsychiatr Dis Treat. 2015;11:853-862.

15. Mihaljević-Peleš A, Šagud M. Klinička obilježja i dijagnoza psihotičnih poremećaja. In: Mihaljević-Peleš A, Šagud M., ed. Antipsihotici u kliničkoj praksi. Zagreb: Medicinska naklada, 2012;1-9.
16. Svjetska zdravstvena organizacija. Međunarodna klasifikacija bolesti i srodnih zdravstvenih problema. 10. Revizija. In: Kuzman M., ed. 2. Izdanje. Zagreb: Medicinska naklada, 2014.
17. Američka psihijatrijska udruga. DSM V. In: Jukić V, Arbanas G., ed. Zagreb: Naklada Slap, 2014.
18. Miller B, Buckley P. Schizophrenia. In: Bope ET, Kellerman RD., ed. Conn`s Current Therapy 2017. Amsterdam: Elsevier, 2017;747-751.
19. Arumugham SS, Thirthalli J, Andrade C. Efficacy and safety of combining clozapine with electrical or magnetic brain stimulation in treatment-refractory schizophrenia. Expert review of clinical pharmacology, journal; 2016;9(9):1245-1252.
20. Zervas IM, Theleritis C, Soldatos CR. Using ECT in schizophrenia: A review from a clinical perspective. World J Biol Psychiatry 2012;13(2):96-105.
21. Mihaljević-Peleš A, Šagud M. Klinička obilježja i dijagnoza afektivnih poremećaja. In: Mihaljevć-Peleš, Šagud M., ed. Antidepresivi u kliničkoj praksi. Zagreb: Medicinska naklada, 2014;1-11.
22. Kornstein SG, Schneider RK. Clinical Features of Treatment-Resistant Depression. J Clin Psychiatry 2001;62 Suppl 16:18-25.
23. Popeo DM. Electroconvulsive therapy for depressive episodes: a brief review. Geriatrics 2009;64:9-1.
24. Reus VI. Bipolar Disorder. In: Alvero R, Ferri FF et al., ed. Ferri`s Clinical Advisor. Amsterdam: Elsevier, 2017;173-174.
25. Bipolar disorder. Definition. Available at: https://www.nimh.nih.gov/health/topics/bipolar-disorder/index.shtml
26. Weissman MM, Bland RC, Canino GJ, Faravelli C, Greenwald S, Hwu HG et al. Cross-national epidemiology of major depression and bipolar disorder. JAMA. 1996;276(4):293-299.
27. Bipolarni poremećaj. Available at: http://www.msd-prirucnici.placebo.hr/msd-prirucnik/pedijatrija/dusevne-bolesti-djece-i-adolescenata/bipolarni-poremecaj
28. Black DW, Winokur G, Nasrallah A. Treatment of mania: a naturalistic study of electroconvulsive therapy versus lithium in 438 patients. J Clin Psychiatry 1987;48:132–139.

29. Marčinko D. Suicidalnost i psihotični poremećaji. In: Mihaljević-Peleš A, Šagud M, ed. Antipsihotici u kliničkoj praksi. Zagreb: Medicinska naklada, 2012;41-48.
30. Marčinko D. Suicidologija. Zagreb: Medicinska naklada, 2011.
31. World Health Organization. Mental health: suicide prevention. Available at: http://www.who.int/mental_health/suicide-prevention/en/
32. Schaffer A, Isometsä ET, Tondo L, Moreno DH, Sinyor M, Kessing LV et al. Epidemiology, neurobiology and pharmacological interventions related to suicide deaths and suicide attempts in bipolar disorder: Part I of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder. Aust N Z J Psychiatry 2015;49(9):785-802.
33. Hor K, Taylor M. Suicide and schizophrenia: a systematic review of rate and risk factors. J Psychopharmacol. 2010;24(4_supplement):81–90.
34. Holmes L. What are suicide rate in the U.S.? Available at: http://mentalhealth.about.com/cs/depression/a/suiciderates.htm
35. Voracek M, Loibl LM. Genetics of suicide: a systematic review of twin studies. Wien Klin Wochenschr. 2007;119(15-16):463-475.
36. Arumugham SS, Thirthalli J, Andrade C. Efficacy and safety of combining clozapine with electrical or magnetic brain stimulation in treatment-refractory schizophrenia. Expert review of clinical pharmacology, journal; 2016;9(9):1245-1252.
37. Caroff SN. The neuroleptic malignant syndrome. J Clin Psychiatry 1980;41:79-83.
38. Aronson JK.Neuroleptic drugs (Neuroleptic malignant syndrome). In: Aronson JK., ed. Meyler`s Side Effects of Drugs. 16th edition. Amsterdam: Elsevier, 2015;53-119.
39. Janović Š, Bajs Janović M. Farmakoterapjija hitnih stanja u psihijatriji. In: Mihaljević-Peleš A, Šagud M., ed. Antipsihotici u kliničkoj praksi. Zagreb: Medicinska naklada, 2012;99-107.
40. Manu P. Medical Consultation in Psychiatry. In: Goldman L, Schafer AI. Goldman-Ceil Medicine., ed. 25th edition. Philadelphia: Elsevier, 2016;2625-2629.
41. Sachdev P, Manson C, Hadzi-Pavlovic D. Case-control study of neuroleptic malignant syndrome. Am J Psychiatry 1997;154(8):1156-1158.
42. Sherchan S, Joshi D. Clinical and demographic profile of patients receiving ECT in an institute. J Nepal Health Res Counc. 2009;7(14):10-13.
43. Adhikari SR, Pradhan SN, Sharma SC, Shrestha BR, Shrestha S, Tabedar S. Diagnostic variability and therapeutic efficacy of ECT in Nepalese sample. Kathmandu University Medical Journal 2008;6(1):41-48.

44. Chanpattana W, Kramer BA, Kunigiri G, Gangadhar BN, Kitphati R, Andrade C. A survey of the practice of electroconvulsive therapy in Asia. J ECT. 2010;26:5–10.
45. Damm J, Eser D, Schüle C, Obermeier M, Möller HJ, Rupprecht R, et al. Influence of age on effectiveness and tolerability of electroconvulsive therapy. J ECT. 2010;26(4):282-288.
46. Schweder LJ, Lydersen S, Wahlund B, Bergsholm P, Linaker OM. Electroconvulsive therapy in Norway: rates of use, clinical characteristics, diagnoses, and attitude. J ECT. 2011;27(4):292-295.
47. Leiknes KA, Schweder LA, Hoie, B. Contemporary use and practice of electroconvulsive therapy worldwide. Brain and Behavior 2012;2:283–344.
48. Gazdag G, Dragasek J, Takacs R, Lookene M, Sobow T, Olekseev A, Ungvari GS. Use of Electroconvulsive Therapy in Central-Eastern European countries: an overview. Psychiatrica Danubina 2017;29(2):136-140.
49. Kim HS, Kim SH, Lee NY, Youn T, Lee JH, Chung S, Kim YS, Chung IW. Effectiveness of Electroconvulsive Therapy Augmentation on Clozapine-Resistant Schizophrenia. Psychiatry Investig. 2017;14(1):58-62.
50. Spiric Z, Stojanovic Z, Samardzic R, Milovanović S, Gazdag G, Marić NP. Electroconvulsive therapy practice in Serbia today. Psychiatr Danub. 2014;26(1):66-69.
51. Kolar D. Current status of electroconvulsive therapy for mood disorders: a clinical review. Evid Based Ment Health. 2017;20(1):12-14.
52. Subedi S, Aich TK, Sharma N. Use of ECT in Nepal: A One Year Study From the Country's Largest Psychiatric Facility. J Clin Diagn Res. 2016;10(2):VC01-VC04.
53. Phutane VH, Thirthalli J, Kesavan M, Kumar NC, & Gangadhar BN. Why do we prescribe ECT to schizophrenia patients? Indian Journal of Psychiatry 2011;53(2):149-151.
54. Gazdag, G, Sebestyen G, Zsargo E, Tolna J, Ungvari GS. Survey of referrals to electroconvulsive therapy in Hungary. World J Biol Psychiatry 2009;10(4 Pt 3):900-904.
55. Mihaljević-Peleš A, Bajs Janović M, Stručić A, Janović Š. Analysis of ECT Indications in the Hospitalized Psychiatric Patients. Poster presented at EPA 2017, 25th European Congress of Psychiatry, Florence, Italy, 2017.
56. Leiknes KA, Jarosh-von Schweder L, Hoie B, Contemporary use and practice of electroconvulsive therapy worldwide. Brain Behavior 2012;2(3):283-344.

57. Bloch Y, Ratzoni G, Sobol D, Mendlovic S, Gal G, Levkovitz Y. Gender differences in electroconvulsive therapy: a retrospective chart review. Journal of affective disorders 2005;84(1):99-102.
58. Pinna M, Manchia M, Oppo R, Scano F, Pillai G, Loche AP, Salis P, Minnai GP. Clinical and biological predictors of response to electroconvulsive therapy (ECT): a review. Neurosci Lett. 2016:pii: S0304-3940(16)30801-1.
59. Uchida T, Kishimoto T, Koreki A, Nakao S, Owada A, Koizumi T, Saito A, Sato M, Sawada S, Matsuzaki R, Petrides G, Mimura M. Predictors of readmission after successful electroconvulsive therapy for depression: a chart review study. Int J Psychiatry Clin Pract. 2016;20(4):260-264.
60. Lin H, Liu S, Hsieh MH, Chien Y, Chen I, Liao S, Tsai H, Wu C, Impacts of Electroconvulsive Therapy on 1-year outcomes in patients with schizophrenia: a controlled, population-based mirror-Image study, Schizophrenia Bulletin 2017;43(5).

**BIOGRAPHY**

Ana Stručić was born in 1993, in Zadar to a big family of engineers, mathematicians, thinkers, language lovers, painters, and athletes. In her early life she developed a passion for music, so when she was only 4 years old she was already a part of the children city choir. However, the music was not her only passion. She learned to read pretty early, thirsty for knowledge, after putting a lot of pressure on her parents she entered regular school as well as the primary musical school when she was only 6 years old. During the regular high school education, she felt drawn to psychology and the diseases and states of mind. In order to assess the level of her knowledge and compare it to her peers her psychology teacher and mentor persuaded her to compete, so she won the first prize on the county level in 2010. Unfortunately, from there no competition was organized on the state level. Since then, Ana knew that psychology is something that makes her soul awake. Approximately at the same time, Ana discovered wonders of human body and genetics, so in 4th grade of high school, the natural and logical decision was to combine two passions. After 12 years of education and 11 years of violin together with 4 years of piano playing she successfully graduated at the age of 17 from 2 high schools and at the same time, she enters the University of Zagreb, Medical school in English. She was the first one in her family to go into the field of medicine, however, thankfully, not the only one.

During the student days, she actively participated in CROSS (Croatian Student Summit, 2018) as a workshop leader on the topic of mental health, as well as on Awareness week organized by Debate club of Zagreb Economy faculty (April 2018), on the same topic of mental health. She was also part of the organization committee for the symposium about mental health ("Pogled u sebe", November 2017), as well as part of the organization committee for the Medical Student's Ball (April 2018). During the academic year 2017/2018, on weekly basis, together with her colleague Anica Sabljić she was holding workshops about mental health in two classes in secondary school in Zagreb (Electrotechnical secondary school), as a part of a pilot project "Pogled u Sebe – Mental Health in adolescents" that should help get mental health education in every secondary school in Croatia.

One of her favorite successes in psychiatry field so far happened in April, 2017, as an e-poster that she was working on together with her wonderful and supporting mentors (prof. dr. sc. Alma Mihaljević-Peleš, assistant professor dr. sc. Maja Bajs Janović and assistant professor dr. sc. Šprio Janović) was presented on 25$^{th}$ European Congress of Psychiatry. Another great success, in her opinion, happened in May 2018, when she got published in "Psychiatrica

Danubina" for the first time as one of the authors next to the names of her role models and mentors above mentioned.

Ana kept her mind open to everything that was happening in medicine; still, psychiatry was and is something that always stayed her number one when it comes to choosing the specialty. In the great hope that she will continue down that road, she finds daily peace and satisfaction in meditation, yoga, cycling and salsa dancing.