Comparative Empirical Analysis of Challenging Inpatients under the Medical Treatment and Supervision Act and the Mental Health and Welfare Act

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Background : Psychotic symptoms leading to self-harm and harm to others are a critical concern in treatment. This study aimed to investigate the characteristics and treatment methods of difficult-to-treat patients under the Medical Treatment and Supervision Act (MTSA) and long-term involuntary inpatients under the Mental Health and Welfare Act and assess the impact of the MTSA on psychiatric treatment.

Methods : Data were collected from 233 inpatients (179 men and 44 women) under the MTSA and 65 inpatients (58 men and 7 women) who were involuntarily hospitalized for ＞18 months due to the risk of self-harm or harm to others under the Mental Health and Welfare Act. We compared basic demographics and pharmacotherapy between the 102 inpatients under the MTSA and 53 inpatients under the Mental Health and Welfare Acts with psychotic disorders.

Results : Difficult-to-treat cases under the MTSA included 82 grievous bodily harm cases (35 %), 80 murder cases (34 %), 48 arson cases (21 %), and cases of other offenses. Psychotic disorders were the most frequent primary diagnosis (85 %), and comorbid psychiatric disorders were present in 68 cases (25.8 %). In contrast, long-term hospitalizations under the Mental Health and Welfare Act were predominantly due to schizophrenia (80 %). Comparative analysis of pharmacotherapy revealed higher usage of clozapine in the MTSA group and antipsychotic and anti-parkinsonian medications in the Mental Health and Welfare Act group.

Conclusion : These findings suggest that the MTSA encourages a reduction in the use of multiple antipsychotics and the adoption of clozapine in treatment regimens. *Shinshu Med J 72 : 95—105, 2024*

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Key words : psychotic symptoms, Medical Treatment and Supervision Act, Mental Health and Welfare Act, difficult-to-treat patients

I Introduction

Managing patients with severe psychotic symptoms who are at risk of self-harm or harming others is notably challenging. In Japan, two legislative acts, the Medical Treatment and Supervision Act (MTSA) and the Mental Health and Welfare Act, govern the hospitalization of such patients. The MTSA emphasizes social rehabilitation through a therapeutic alliance between patients and medical personnel, targeting individuals involved in specific crimes, such as murder and arson[1)]. The aim is to reintegrate them into society within the recommended hospitalization period of approximately 1.5 years **(Fig. 1)**. However, some patients have been hospitalized for extended periods[2)]. Such prolonged hospitalization can be attributed to a

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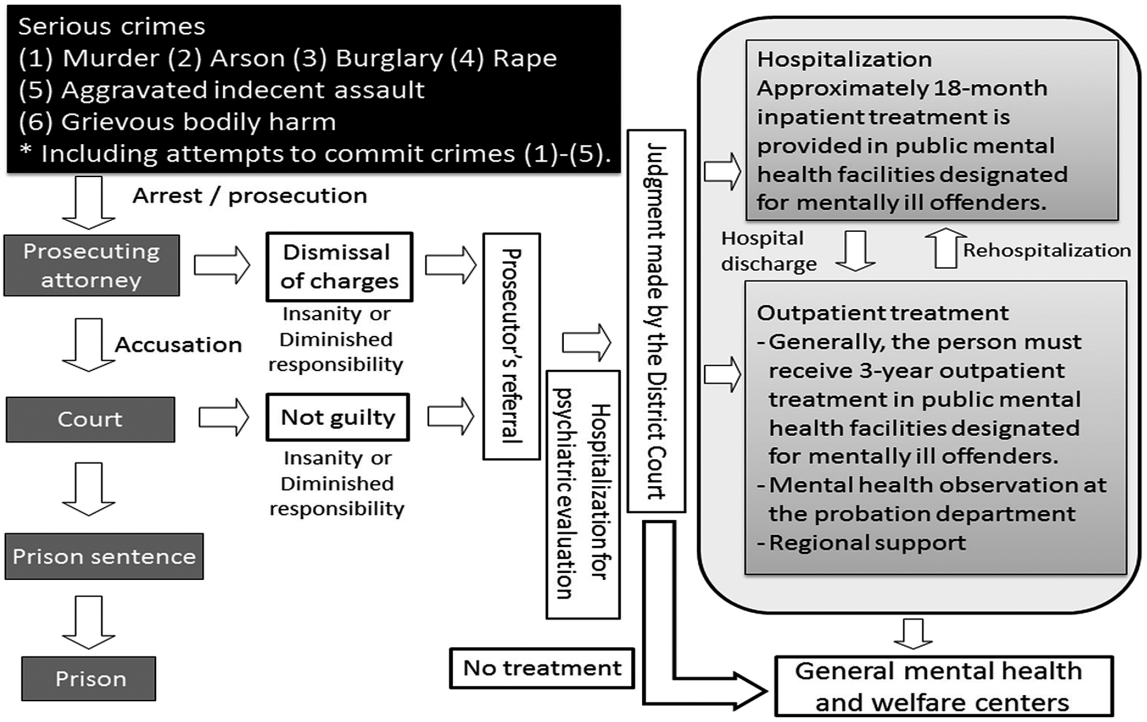

Fig. 1　Structure of the Medical Treatment and Supervision Act
This diagram (translated from the Japanese version available online[1]) illustrates the structure of the Medical Treatment and Supervision Act.

variety of complex factors beyond inherent psychotic symptoms, such as coexisting disorders and social challenges[3]. Understanding these cases could significantly enhance the psychiatric treatment under the MTSA. In contrast, the Mental Health and Welfare Act allows involuntary hospitalization of individuals with mental disorders who pose a risk of self-injury or harm to others. Once their condition improves, these patients are typically discharged, facilitating their reintegration into society. Retrospective cohort studies[4] showed that 97 % of the patients hospitalized due to risks of self-harm or harm to others were discharged within 180 days, while approximately 3 % remained hospitalized for an extended duration. Such extended hospital stays are a notable concern in psychiatric treatment.

Compared to general psychiatric treatment, MTSA psychiatric treatment involves a multidisciplinary team and employs specialized therapies, such as clozapine and electroconvulsive therapy (ECT), for treatment-resistant schizophrenia. The active promotion of these therapies aims to enhance treatment responsiveness[5].

In an effort to understand challenging cases in psychiatry, this study aimed to examine difficult-to-treat cases under the MTSA (hereinafter referred to as "difficult-to-treat cases") and those with prolonged hospitalization under the Mental Health and Welfare Act due to risks of self-harm and harm to others. Additionally, we assessed the impact of the MTSA on psychiatric treatment based on patient characteristics and treatment methods.

Ⅱ　Methods

A　Difficult-to-treat cases under the MTSA

We defined a case as a difficult-to-treat case if at least one of the following criteria was applicable, as described by Hirabayashi[3] : (1) hospitalized for ＞6 years, (2) requiring frequent isolation (≥5 times since admission), (3) requiring long-term isolation (≥28 days since admission), (4) requiring physical restraints (at least once since admission), (5) re-hospitalized, and (6) re-treated under the MTSA. Rehospitalization was defined as readmission due to a deterioration in the patient's condition or problematic behavior during

outpatient treatment, while retreatment referred to hospitalization due to the occurrence of a new target act.

We conducted a detailed survey of hospitalized patients who met the criteria for being difficult to treat. Questionnaires were distributed to designated inpatient institutions across Japan under the MTSA. The following information was collected : age, sex, diagnosis, nature of the target act, admission date, the status of post-discharge medical care arrangements, economic status, challenges in treatment and discharge, rationale and objectives for the latest petition for continued hospitalization, a summary of medical treatment and illness progression in the past six months, and the use of clozapine or ECT. Participants were requested to input these data into the survey. The collected questionnaires were analyzed quantitatively and qualitatively using the textual data from hospitalization continuation sheets. A report, submitted to the court every six months by designated inpatient facilities, serves as the basis for judicial decisions regarding treatment. Between 2016 and 2017, data were collected from 26 out of the 33 designated inpatient institutions that existed in Japan at the time, and a total of 233 patients (179 men and 44 women) were included in the analysis. The collected data included various parameters : sex, age at admission, age at the time of the survey, Intelligence Quotient (IQ) score (assessed using the Wechsler Adult Intelligence Scale 3rd edition), use of clozapine, history of ECT treatment, instances of physical restraints and isolation, diagnosis, and details about the victimization of the target act. Multiple diagnoses were allowed for comorbid disorders.

B Long-term hospitalized inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

Seto et al.[4] conducted a preliminary survey of 1,386 hospitals, including national hospitals with psychiatric wards (n = 28), public hospitals with psychiatric wards (n = 139), hospitals affiliated with the Japan Psychiatric Hospital Association (n = 1,208), and other hospitals with high-standard specialized psychiatric wards that play a central role in psychiatric emergency care under the public medical insurance system (n = 11). As noted by Seto et al.[4], as of June 30, 2017, 65 patients had been hospitalized for more than 18 months under the Mental Health and Welfare Act because of risks of self-harm and harm to others. Permission to use these data for this study was obtained from Seto et al..

In this study, questionnaires were distributed to those hospitals that expressed willingness to participate. Additionally, notices were placed in the wards to inform patients that they had the option to decline participation in the study. Of the 1,386 hospitals, 686 (49.5 %) responded to the preliminary survey. Of these, 62 institutions reported a total of 122 cases of long-term hospitalization. Subsequently, questionnaires were mailed to 87 patients from 38 participating medical institutions, and responses were received from 75 patients (58 men and 17 women) across 34 institutions. We collected data on age, sex, diagnosis, treatment history, instances of serious harm, current problematic behavior, current symptoms and conditions, current activity restrictions, treatment status and plans, instances of temporary hospital discharge, and medication usage.

C Comparative analysis of pharmacotherapy in schizophrenia between difficult-to-treat patients under the MTSA and long-term hospitalized inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

Of the 233 difficult-to-treat cases, 119 had hospital stays exceeding 18 months. Among the 119 difficult-to-treat cases under the MTSA and 65 cases in the long-term hospitalization group under the Mental Health and Welfare Act, 102 and 53 were primarily diagnosed with psychotic disorders, respectively. The following data were collected for both groups : sex, age at the time of the survey, percentage of clozapine use, percentage of ECT use, the number of oral and antipsychotic medications, chlorpromazine equivalent dose, the number of benzodiazepine medications and their diazepam equivalent dose, the number of antidepressant medications and their imipramine equivalent dose, and the number of anti-parkinsonian drugs and their biperiden equivalent dose.

Comparisons between the two groups were per-

Table 1 Demographic and clinical characteristics of difficult-to-treat cases

	Murder	Arson	Burglary	Aggravated indecent assault	Grievous bodily harm	Total
	n = 80	n = 48	n = 11	n = 12	n = 82	n = 233
Sex						
Male	65 (81 %)	30 (63 %)	9 (82 %)	12 (100 %)	70 (85 %)	179 (80 %)
Female	15 (19 %)	18 (38 %)	2 (18 %)	0 (0 %)	12 (15 %)	44 (20 %)
Age at admission	42.5 (12.3)	43.0 (10.4)	37.9 (11.7)	44.2 (12.1)	41.6 (11.6)	42.1 (11.5)
Age at time of survey	45.1 (11.9)	45.1 (10.5)	40.6 (10.9)	47.1 (12.0)	44.1 (11.4)	44.6 (11.4)
Full scale IQ	82.5 (17.2)	72.8 (16.8)	64.2 (12.1)	64.4 (17.6)	82.2 (15.9)	77.0 (19.9)
CLZ usage rate	31 (39 %)	20 (42 %)	2 (18 %)	4 (33 %)	36 (44 %)	93 (40 %)
ECT usage rate	8 (10 %)	5 (10 %)	0 (0 %)	0 (0 %)	8 (10 %)	21 (9 %)
Seclusion	31 (39 %)	23 (48 %)	5 (46 %)	1 (8 %)	35 (43 %)	95 (41 %)
Medical restraint	13 (16 %)	7 (15 %)	8 (73 %)	2 (17 %)	10 (12 %)	40 (17 %)

Data are shown as mean (standard deviation) or the number of patients (frequency).
CLZ : clozapine ; ECT : electroconvulsive therapy

formed using the t-test for continuous variables and Fisher's exact test for categorical data. Statistical significance was defined as a two-tailed $P < 0.05$. Statistical analyses were performed using the R software (version 4.2.1).

D Ethical considerations

Data were collected from relevant medical institutions, and no personal identification was collected. Informed consent was not required given the deidentified nature of the data. This study was reviewed and approved by the Research Ethics Committee of the Komoro Kogen Hospital on August 23, 2021 (Ethics Committee Approval No. 3-3).

Ⅲ Results

A Difficult-to-treat cases under the MTSA

1 Clinical and demographic characteristics of difficult-to-treat cases

Clinical and demographic characteristics of the patients are shown in **Table 1**. The sex ratio was 4.1 : 1, which is higher than the 3.3 : 1 ratio reported in the 2020 MTSA Statistics[4] for all MTSA hospitalization cases in Japan. Specifically, for cases of sexual assault, the proportion of male patients was 100 % , while for arson, a higher proportion of female patients was noted in the MTSA than in other types of target acts. The mean age at admission (standard deviation [S.D.]) was 42.1 (11.5) years.

The mean IQ score (S.D.) was highest for murder cases at 82.5 (17.2) and lowest for burglary cases at 64.2 (12.1). A histogram illustrating the distribution of IQ scores across all cases is shown in **Fig. 2.** Regarding treatment, clozapine was administered to 40.0 % of cases, whereas ECT was employed in 9.0 % of cases. Isolation was implemented in 41.0 % of cases, and physical restraint was used in 17.2 % of cases. Notably, physical restraints were most frequently employed in burglary cases.

2 Primary diagnosis and comorbid disorders

The primary diagnoses were frontotemporal lobe dementia (ICD-10 Code : F02) in one case, organic delusional disorder (F06) in two cases, substance use disorder (F1X) in seven cases, schizophrenia (F20) in 184 cases, delusional disorder (F22) in four cases, acute polymorphic psychotic disorder with schizophrenic symptoms (F23) in one case, schizoaffective disorder (F25) in ten cases, bipolar affective disorder (F31) in seven cases, depression (F32) in three cases, moderate recurrent depressive disorder (F33) in one case, mixed anxiety and depression disorder (F41) in one case, personality disorder (F60) in two cases, mild intellectual disability (F70) in one case, moderate intellectual disability (F71) in two cases, and pervasive developmental disorder (F84) in seven cases **(Table 2)**.

Comorbid disorders were diagnosed in 68 cases (28.5 %). Specifically, the comorbid conditions included

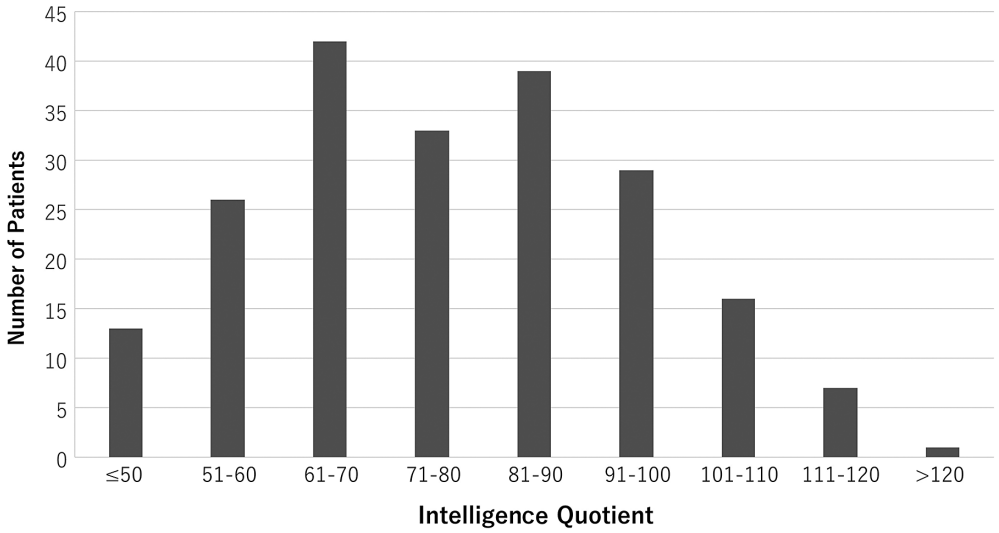

Fig. 2 Histogram of total test IQ
A histogram of total test IQ in difficult-to-treat cases is shown.

Table 2 Main diagnosis and supplementary diagnosis in ICD-10 codes of difficult-to-treat cases

	Murder n = 80	Arson n = 48	Burglary n = 11	Aggravated indecent assault n = 12	Grievous bodily harm n = 82	Total n = 233
Main diagnosis						
F00-09			1 (9 %)		2 (2 %)	3 (1 %)
F10-19	3 (4 %)		3 (27 %)		1 (1 %)	7 (3 %)
F20-29	70 (88 %)	40 (83 %)	7 (64 %)	11 (92 %)	71 (87 %)	199 (85 %)
F30-39	4 (5 %)	4 (8 %)			3 (4 %)	11 (5 %)
F40-49	1 (1 %)				1 (1 %)	2 (1 %)
F70-79	1 (1 %)	1 (2 %)		1 (8 %)	1 (1 %)	4 (2 %)
F80-89	1 (1 %)	3 (6 %)			3 (4 %)	7 (3 %)
Supplementary diagnosis						
F00-09		1 (2 %)				1 (2 %)
F10-19	4 (5 %)		2 (18 %)		3 (4 %)	9 (13 %)
F20-29	2 (3 %)				1 (1 %)	3 (4 %)
F40-49					2 (2 %)	2 (3 %)
F60-69		1 (2 %)		1 (8 %)		2 (3 %)
F70-79	4 (5 %)	9 (19 %)	2 (18 %)	1 (8 %)	9 (11 %)	25 (37 %)
F80-89	5 (6 %)	4 (8 %)		3 (25 %)	5 (6 %)	17 (25 %)
F90-99	2 (3 %)	1 (2 %)	1 (9 %)	1 (8 %)	2 (2 %)	7 (10 %)
Others					2 (2 %)	2 (3 %)

Numbers indicate the number of pateints (frequency).

organic mental disorder (F09) in one case, substance use disorder in nine cases, schizophrenia (F20) in three cases, obsessive-compulsive disorder (F42) in two cases, personality disorder in one case, sexual preference disorder (F65) in one case, mild intellectual disability in 18 cases, moderate intellectual disability in five cases, unspecified intellectual disabilities (F79) in two cases, pervasive developmental disorder in seventeen cases, attention deficit hyperactivity disorder (F90) in 6 cases, Gilles de la Tourette syndrome

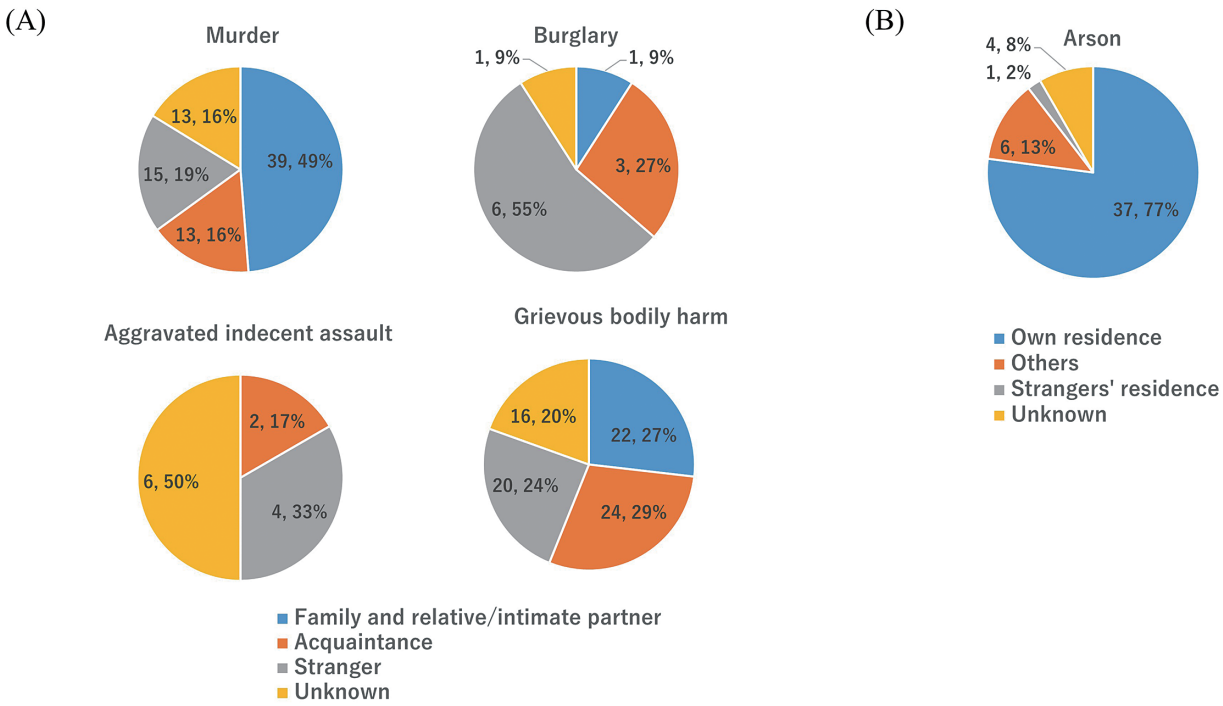

Fig. 3　Criminal types and victims
(A) Victim categories of murder, burglary, sexual assault, and grievous bodily harm are presented.
(B) The target category of the arson is shown.
The numbers shown in the pie charts indicate the count and percentage of patients.

(F95) in one case, hyponatremia (E87) in one case, and 22q11.2 deletion syndrome in one case. Notably, cases of burglary showed a notably high proportion of both primary and comorbid diagnoses with the ICD-code F10-19 **(Table 2)**.

3　Target act, victim type, and victim classification

In the 233 difficult-to-treat cases, the breakdown of target acts was as follows : 80 cases of murder (comprising 43 murder attempts) (34 %, 95 % CI : 28-40 %), 48 cases of arson (including 7 attempts) (21 %, 95 % CI : 15-25 %), 11 cases of burglary (including 5 attempts) (5 %, 95 % CI : 2-7 %), no instances of rape, 12 cases of aggravated indecent assault (including 1 attempt) (5 %, 95 % CI : 2-8 %), and 82 cases of grievous bodily harm (35 %, 95 % CI : 29-41 %).

Fig. 3 shows the victim categories for murder, burglary, sexual assault, and grievous bodily harm, as well as the target categories for arson. Among the 80 murder cases, two incidents involved the killing of multiple family members : one case was the murder of a mother and another relative, while the other case involved a father and his siblings. The most frequently targeted family member was the mother, with 15 cases, followed by the father in 11 cases. Additionally, siblings were the victims in three cases, children in three cases, and a spouse in one case.

Among the 82 cases of grievous bodily harm, the identity of the victims was unknown in 23 instances. Fathers were the victims in 10 cases, while mothers were targeted in seven cases. Spouses were the victims in four cases, and children were involved in one case.

Arson was most commonly committed in a home setting.

B　Long-term hospitalized inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

Clinical and demographic characteristics of these patients are shown in **Table 3**. The proportion of males was higher than that of females. More than 80 % of the primary diagnoses were schizophrenia. The usage of clozapine among patients was 7 % , while 13 % received ECT.

Table 3 Demographic and clinical characteristics, main diagnosis, and supplementary diagnosis of long-term inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

Variable	Long-term inpatients at risk of self-harm or harming others n = 65	ICD-10	Main diagnosis n = 65	Supplementary diagnosis n = 20
Sex		F00-09	3 (5 %)	1 (5 %)
Male	58 (89 %)	F10-19	4 (6 %)	1 (5 %)
Female	7 (11 %)	F20-29	53 (82 %)	1 (5 %)
Age at admission	42.1 (12.9)	F30-39	1 (2 %)	1 (5 %)
Age at time of survey	52.0 (13.6)	F60-69	1 (2 %)	5 (25 %)
CLZ usage rate	5 (7 %)	F70-79	1 (2 %)	9 (45 %)
ECT usage rate	10 (13 %)	F80-89	2 (3 %)	2 (10 %)

Data are shown as mean (standard deviation) or the number of patients (frequency).
CLZ : clozapine ; ECT : electroconvulsive therapy

Table 4 Comparison of pharmacotherapy for patients with schizophrenia : difficult-to-treat patients under the MTSA vs. long-term inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

Variable	Difficult-to-treat cases n = 102	Long-term inpatients at risk of self-harm or harming others n = 53	Statistics
Sex			
Male	81 (79 %)	46 (87 %)	p = 0.282 †
Female	21 (21 %)	7 (13 %)	
Age at time of survey	44.1 (10.5)	52.7 (13.9)	t = −4.30, df = 153, p < 0.05
CLZ usage rate	48 (47 %)	2 (3.8 %)	p < 0.05 †
ECT usage rate	12 (12 %)	10 (19 %)	p = 0.236 †
Number of oral medications	5.4 (3.2)	6.4 (2.9)	t = −1.86, df = 153, p = 0.065
Number of antipsychotics	1.6 (0.9)	2.2 (1.1)	t = −3.25, df = 153, p < 0.05
Chlorpromazine equivalent	917.1 (588.3)	1019.2 (678.2)	t = −0.97, df = 153, p = 0.332
Number of benzodiazepines	0.9 (0.9)	1.2 (1.1)	t = −1.28, df = 153, p = 0.201
Diazepam equivalent	10.2 (14.5)	11.4 (12.6)	t = −0.5, df = 153, p = 0.618
Number of antidepressants	0.1 (0.3)	0	
Imipramine equivalent	11.2 (36.2)	–	
Number of antiparkinsonian drugs	0.3 (0.6)	0.5 (0.5)	t = −2.01, df = 153, p < 0.05
Biperiden equivalent	0.8 (1.9)	1.6 (2.0)	t = −2.33, df = 153, p < 0.05

Data are shown as mean (standard deviation) or the number of patients (frequency).
CLZ : clozapine ; ECT : electroconvulsive therapy
† Fisher's exact test

C Comparison of pharmacotherapy in schizophrenia between difficult-to-treat patients under the MTSA and long-term inpatients at risk of self-harm or harming others under the Mental Health and Welfare Act

The number of antipsychotic medications and anti-Parkinsonian medications, as well as the diazepam equivalent doses of benzodiazepines, was higher in the long-term inpatient group **(Table 4)**. No significant difference was observed in the chlorpromazine equivalent doses of antipsychotics between the two groups.

Ⅳ Discussion

The treatment of patients with psychotic symptoms, which can lead to self-harm and harm to others, is a critical challenge in psychiatric care. This study focused on difficult-to-treat inpatients under the MTSA

and long-term inpatients under the Mental Health and Welfare Act who were at risk of self-harm or harm to others. These groups represent the most severe cases in the field of psychiatry. The majority of difficult-to-treat inpatients under the MTSA and long-term hospitalization cases under the Mental Health and Welfare Act were male patients with schizophrenia. Murder and grievous bodily harm were the most common target acts for patients under the MTSA. Clozapine was used in a higher proportion of patients treated under the MTSA.

Collecting and analyzing data on cases under the MTSA and involuntarily admitted inpatient cases under the Mental Health and Welfare Act due to the risk of self-harm or harm to others is challenging due to stringent information management protocols. To the best of our knowledge, no similar studies have been published to date.

No significant differences were found in patient demographics between the difficult-to-treat cases in the present study and those reported in the 2020 MTSA statistical data[6], which encompassed 3,761 patients hospitalized from the enactment of the MTSA until December 31, 2020. The proportions of the target acts in the difficult-to-treat cases in the present study were similar to those in previous data.

In difficult-to-treat cases, the patients were predominantly male, and their average age at admission was in the early 40s, similar to the demographics reported in the 2020 MTSA statistical data. The length of hospital stay often exceeded the MTSA's goal (1.5 years). The mean IQ score was 77.0, indicating that many patients were in the borderline intelligence range. Some patient groups showed higher rates of intellectual disability, whereas others exhibited intelligence within the typical range **(Fig. 2)**.

Research on the relationship between IQ and criminal behavior is limited. Some reports propose that individuals with schizophrenia and below borderline intellectual functioning may experience more severe psychotic symptoms[7]. The behaviors of those with intellectual disabilities might be more susceptible to delusions, potentially leading to impulsive criminal activities. Conversely, instances where actions stem from nervousness, anguish, anxiety, and hopelessness are suggested to be associated with relatively higher intelligence. Further studies with an increased sample size are necessary to confirm the trends in IQ scores among various patient categories.

The most common diagnosis in difficult-to-treat cases was schizophrenia, and many patients had comorbid disorders. Intellectual disability was the most prevalent comorbidity, followed by pervasive developmental disorders. Patients with comorbid schizophrenia and intellectual disability encounter significant obstacles in their treatment[8]. While it is possible to manage psychotic symptoms such as hallucinations and delusions to some extent through treatment, the presence of intellectual disabilities, autistic traits, and problematic behaviors, such as difficulties with impulse control, presents significant challenges in the overall treatment process.

In murder cases, victims tended to have a close relationship with the perpetrator, whereas in cases of burglary, sexual assault, and grievous bodily harm, the majority of victims were usually unknown or strangers to the perpetrator. The targets of arson were predominantly the patient's own residences, indicating a potential association with attempted suicide. Higher suicidality has been reported in individuals with mental disorders who commit arson[9]. Associations between psychiatric symptoms and the targets of the crime should be explored in future studies.

In the long-term hospitalization group, many patients were primarily diagnosed with schizophrenia under the Mental Health and Welfare Act. Among these long-term hospitalized individuals, 31 % had comorbid diagnoses. Seto et al.[4] showed that "difficulty in symptom improvement" and "inadequate impulse control" were the most common reasons for the challenges in discharging patients who were involuntarily hospitalized due to risks of self-harm and harming others and that many of these patients had hallucinations, delusions, and impulse control problems. In managing these conditions, patients often receive high doses of antipsychotic drugs and are commonly prescribed two or more medications de-

spite experiencing no significant improvement in symptoms, highlighting the complexities and challenges in treating these cases.

In a survey of 10,106 inpatients with schizophrenia conducted by the Japanese Psychiatric Clinical Pharmacy Research Group[10], it was found that the average number of antipsychotic drugs was 1.7, with a mean chlorpromazine-equivalent dose of 722 mg/day. In contrast, the chlorpromazine-equivalent dose was higher in difficult-to-treat schizophrenia patients in the present study.

The prevalent use of multiple antipsychotic medications and anti-parkinsonian drugs in long-term hospitalized inpatients under the Mental Health and Welfare Act suggests that each antipsychotic was typically prescribed at a relatively low dose. In contrast, the proportion of clozapine prescriptions among patients under the MTSA was 47 %, significantly higher than the proportion (3.8 %) in patients under the Mental Health and Welfare Act. The higher rate of clozapine use might have facilitated more effective monotherapy with antipsychotic medications, thereby reducing the need for additional anti-Parkinsonian medications in inpatients under the MTSA. Comparatively, a survey of schizophrenia patients conducted by the Japanese Psychiatric Clinical Pharmacy Research Group[10] found that the percentage of clozapine prescriptions among psychiatric inpatients in Japan was 4.8 %, a figure much lower than the 47 % for inpatients under MTSA.

According to Gaebel et al.[11], clozapine is recommended for treating treatment-resistant schizophrenia. Despite its effectiveness, there's a global trend of underutilization of clozapine[12]. The rates of clozapine prescriptions for both inpatients and outpatients are 4.8 % in the United States[13], 5.5 % in Sweden[14], 8.3 % in Australia[15], 10.1 % in Denmark[16], 10.9 % in South Korea[17], 23.7 % in England and Wales[18], and 24.6 % in China[19]. The reasons for these low prescription rates include the risks of serious side effects, such as agranulocytosis, myocarditis, and intestinal obstruction, and the requirement for continuous hematological monitoring[20]. In Japan, the rate of clozapine prescription was relatively low at 6.2 %[21] owing to the stringent regulations regarding the safe prescription of clozapine compared to other countries. However, in 2021, there was a revision in the package insert to relax these regulations. The Ministry of Health, Labor and Welfare has set a goal to expand the use of clozapine to reach 25 % of patients with treatment-resistant schizophrenia. Despite these efforts, the factors contributing to the low prescription rate of clozapine in Japan remain unclear and warrant further investigation.

Based on our findings, clozapine is used more frequently under the MTSA than in other countries or the broader Japanese medical systems. One reason may be that the guidelines for inpatient treatment under the MTSA recommend the use of clozapine, which has been proven to be effective in severe chronic schizophrenia[22], for patients with treatment-resistant schizophrenia. Additionally, the prevalence of particularly difficult-to-treat cases under the MTSA might necessitate the use of clozapine. However, the chlorpromazine-equivalent dose of antipsychotics was not significantly higher in patients under the MTSA than in those under the Mental Health and Welfare Act in the present study. Notably, the number of prescribed antipsychotics was minimal in inpatients under the MTSA, implying that adherence to treatment guidelines led to monotherapy with antipsychotics, particularly clozapine.

The utilization of ECT was notably higher among participants in the current study compared to patients undergoing general psychiatric treatment[23]. Apart from the substantial number of severely ill patients, this discrepancy may be attributed to the more widespread availability of ECT equipment in designated inpatient facilities compared to general psychiatric hospitals. However, in contrast to the rate of clozapine utilization, the rate of ECT use was not higher for patients under the MTSA than those under the Mental Health and Welfare Act. This could be attributed to a higher preference among patients under the MTSA for continuous treatments such as clozapine, especially when considering the outpatient treatment period. Further studies are warranted to explore the optimal utilization of clozapine and ECT in

patients with treatment-resistant schizophrenia and to actively promote the use of clozapine and ECT, where necessary, to enhance treatment outcomes in these challenging cases.

A Strengths and limitations

The strength of our study lies in the analysis of data from patients hospitalized under the MTSA, a dataset that is often challenging to obtain. Additionally, this study enhances the understanding of medical treatment under the MTSA by comparing these findings with those from patients hospitalized under the Mental Health and Welfare Act.

This study has several limitations that must be noted. First, owing to the stringent confidentiality protocols, data collection was confined to difficult-to-treat and long-term hospitalized inpatients, precluding comparisons with more general cases. Second, clinical scales were not used to assess the illness severity. Third, the survey was originally conducted under a different framework for patients hospitalized under the MTSA and the Mental Health and Welfare Act. Therefore, variations in the survey items and a lack of consistency existed between the two groups. Further examination of problematic behaviors that result in hospitalization is essential to improve discharge support.

V Conclusions

The majority of difficult-to-treat patients under MTSA had schizophrenia. The present findings suggest that appropriate therapeutic strategies, such as monotherapy with antipsychotic drugs and active use of clozapine, are emphasized for inpatients under the MTSA. Learning from the treatment of these difficult-to-treat MTSA cases has the potential to significantly enhance psychiatric care in Japan. In particular, promoting the use of clozapine and ECT may be beneficial for patients who experience prolonged hospitalization due to severe psychotic symptoms and challenges in symptom improvement. Therefore, additional research in this area is warranted to further refine and develop effective treatment strategies.

Conflict of interest

The authors declare that they have no conflict of interest.

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