The Safety and Strategies for Reinitiating Electroconvulsive Therapy (ECT) After ECT-Induced Takotsubo Cardiomyopathy: A Case Report and Systematic Review

Michiko Kinoshita, MD, PhD,[1*] Makoto Kinoshita, MD, PhD,[2] Rikako Takahashi, MD,[1] Sarara Mutoh, MD,[1] Nami Kakuta, MD, PhD,[1] Katsuya Tanaka, MD, PhD[1]

[1] Department of Anesthesiology, Tokushima University Hospital, 2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan

[2] Department of Psychiatry, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-8-15 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan

*** Address for Correspondence and Reprints:** Michiko Kinoshita, Department of Anesthesiology, Tokushima University Hospital, 2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan. Tel.: +81 (0)88-633-7181; Fax: +81 (0)88-633-7182; Email: michiko-kinoshita@tokushima-u.ac.jp

Conflicts of Interest and Source of Funding: The remaining authors have no conflicts of interest or financial disclosures to report.

ABSTRACT

Objectives:

Takotsubo cardiomyopathy (TCM) is a life-threatening complication of electroconvulsive therapy (ECT). We report the case of a 66-year-old woman who was re-challenged with ECT after ECT-induced TCM. Moreover, we have made a systematic review to assess the safety of and strategies for re-initiating ECT after TCM.

Methods:

We searched for published reports on ECT-induced TCM since 1990 in MEDLINE (PubMed), Scopus, Cochrane Library, ICHUSHI, and CiNii Research.

Results:

A total of 24 ECT-induced TCM cases were identified. Patients who developed ECT-induced TCM were predominantly middle-aged and older women. There was no specific trend in anesthetic agents used. Seventeen (70.8%) cases developed TCM by the third session in the acute ECT course. Eight (33.3%) cases developed ECT-induced TCM despite the use of β-blockers. Ten (41.7%) cases developed cardiogenic shock or abnormal vital signs related to cardiogenic shock. All cases recovered from TCM. Eight (33.3%) cases tried to receive ECT retrial. The duration until ECT retrial was between 3 weeks and 9 months. The most common preventive measures during ECT retrial were

related to β-blockers; however, the type, dose, and route of administration of β-blockers varied. In all cases, ECT could be re-performed without TCM recurrence.

Conclusions:

ECT-induced TCM is more likely to cause cardiogenic shock than non-perioperative cases; nevertheless, it has good prognosis. Cautious re-initiation of ECT after TCM recovery is possible. Further studies are required to determine preventive measures for ECT-induced TCM.

Key Words: electroconvulsive therapy, takotsubo cardiomyopathy, case report, systematic review

INTRODUCTION

Takotsubo cardiomyopathy (TCM), also called stress cardiomyopathy, broken heart syndrome, and apical ballooning syndrome, is a non-ischemic cardiomyopathy induced by emotional or physical stress.[1] Over half of patients with TCM have neurological or psychiatric disorders, suggesting an association between neuropsychiatric disorders and TCM.[2] While the mechanism underlying TCM is not yet fully understood, sympathetic stimulation and excess catecholamines are the most likely causes.[3–6] No preventive measures for TCM, including pharmacotherapy, have been established to date.[7]

Electroconvulsive therapy (ECT) is highly effective in treating severe major depressive disorders, bipolar disorders, and schizophrenia.[8–10] ECT safety under general management is considered very high[11]; nevertheless, clinical reports describing ECT-induced TCM have increased. Repeated ECT performance within a short period is essential for therapeutic efficacy in the acute phase,[12] and multiple ECT cycles over an extended period are sometimes necessary to maintain remission and prevent relapse.[13] Hence, once ECT-induced TCM develops, the feasibility and safe performance of ECT retrial in patients with severe psychiatric disorders are crucial; however, they are insufficiently understood.

Herein, we report the case of a 66-year-old woman with ECT-induced TCM who was successfully re-challenged with ECT without TCM recurrence. Additionally, we conducted a comprehensive literature search and summarized the characteristics of previously published cases of ECT-induced TCM. This systematic review aimed to assess the safety of and strategies for re-initiating ECT after TCM. The results of this study can contribute to the perioperative management and understanding of ECT complications.

MATERIALS AND METHODS

Case Report

Written consent was obtained from the patient and her family for the publication of the case report, and the patient's anonymity was carefully protected.

The patient was a 66-year-old female (height: 155.5 cm, weight: 38.3 kg) with a history of depressive episodes (specifically, at the age of 23 years after childbirth and at the age of 45 years upon the death of her brother). One year prior to hospitalization, she experienced anxiety, insomnia, and difficulty concentrating. She also had delusions of belittlement and was diagnosed with severe major depressive disorder, alongside psychotic features. Then, she started receiving medications, specifically vortioxetine

and aripiprazole. Her delusions were partially improved; however, other symptoms persisted. Vortioxetine and aripiprazole were changed to venlafaxine and brexpiprazole, respectively. She was hospitalized due to inadequate response to drug therapy. After hospitalization, lurasidone was combined with venlafaxine. Subsequently, venlafaxine was replaced with escitalopram; mirtazapine was also prescribed but was ineffective. Her Hamilton Rating Scale for Depression (HAM-D) score was 25 points in 17 items and 28 points in 21 items. The first ECT course was scheduled to improve the symptoms. Her medical history included hypertension and transient ischemic attack, whereas her medications included lurasidone, escitalopram, mirtazapine, irbesartan, aspirin, lansoprazole, and linaclotide. Preoperative examination findings revealed a left anterior hemiblock on electrocardiogram (ECG); no other special abnormalities were observed.

Her vital signs before the first ECT session were as follows: heart rate, 70 beats per minute (bpm); blood pressure, 135/80 mmHg. Propofol (40 mg) and succinylcholine (40 mg) were used as anesthetic agents and bilateral pulse-wave ECT produced effective motor and electroencephalogram seizure duration (≥15 s and ≥20 s, respectively). Her heart rate increased to 128 bpm and her tachycardia (>100 bpm) lasted for 234 s after stimulation. Subsequently, her blood pressure increased to 204/87

mmHg, and nicardipine (1 mg) was administered intravenously. There were no complaints, including chest pain or abnormal vital signs, after the first ECT.

She was set to receive the second ECT 2 days after the first ECT session; however, this was canceled because deep negative T-waves were observed in all limb leads of the ECG, although other vital signs were normal and there were no complaints. Her heart rate and blood pressure were 76 bpm and 112/81 mmHg, respectively. Echocardiography revealed full circumferential apex akinesis, basal left ventricular (LV) hypercontractility, and ejection fraction of 34%. Coronary artery and LV angiography revealed characteristic LV dysfunction without lesions in the coronary artery. Troponin I was elevated to 1256 $pg \cdot mg^{-1}$ (reference value, <27 $g \cdot mg^{-1}$). She was diagnosed with TCM according to the Japanese Circulation Society diagnostic criteria,[14] consistent with the Mayo Clinic criteria.[15] There were no subjective symptoms or abnormal vital findings, and no other special treatment was required for TCM. LV systolic dysfunctions faded without challenges. Moreover, there were no obvious wall motion abnormalities at 4 weeks after TCM onset.

Re-initiating ECT was considered because of persistent depressive symptoms after TCM improved. Her HAM-D score was 28 points in 17 items and 33 points in 21 items. Medications included sertraline and olanzapine; administration of irbesartan,

aspirin, lansoprazole, and linaclotide was continued, as before. She and her family chose to resume ECT after a discussion of the risks and benefits of resuming ECT, including the risk of TCM recurrence. In the new ECT session, remifentanil was used with the anesthetic used during the first session. Landiolol, a short-acting β1 selective blocker, was scheduled to be used only if tachycardia persisted after stimulation.

At 6 weeks after TCM onset, a new ECT session was initiated. A bolus dose of 40 ug and a continuous dose of 0.3 $ug \cdot kg^{-1} \cdot min^{-1}$ of remifentanil were administered until stimulation. Furthermore, propofol was reduced to 30 mg, and 40 mg of succinylcholine was administered as before. Her ECG was carefully monitored after ECT, and brief echocardiography was performed after each ECT until the fifth session. Consequently, she could receive 10 ECT sessions without TCM recurrence. Her depressive symptoms were improved; her HAM-D score was 0 points in both 17 and 21 items. In the 10 ECT sessions with remifentanil, the mean systolic blood pressure elevation was 42 mmHg (95% confidence interval [CI]: 32–50). Her mean maximum heart rate was 117 bpm (95% CI: 114–120) and mean tachycardia duration was 38 s (95% CI: 29–47). Landiolol was not needed owing to the short duration of tachycardia.

Ethics

121 This study was registered in the International Prospective Register of
122 Systematic Reviews (PROSPERO; registration number: 336851). This manuscript
123 adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
124 (PRISMA) statement.
125
126 **Information Source and Search Strategy**
127 We conducted a comprehensive literature search using MEDLINE (PubMed),
128 Scopus, Cochrane Library, ICHUSHI (Japan Medical Abstract Society), and CiNii
129 (Citation Information by the National Institute of Informatics) Research. The search
130 strategy included ECT- and TCM-related English and Japanese terms. Details of the
131 search strategy are provided in Supplemental Digital Content 1.
132 The search was conducted between January 1, 1990 and June 1, 2022. No
133 restrictions were set on language or geographic location, and EndNote version 20.3
134 (Clarivate™, London, UK), a literature management software, was used.
135
136 **Eligibility Criteria**
137 Case reports, case series, reviews, studies, letters, and conference reports
138 comprehensively describing the original data of the patients with ECT-induced TCM

were included, and TCM cases that were not triggered by ECT were excluded. In addition, articles providing previously-reported cases were excluded to avoid duplication, as were those without the full text.

Selection Process

After excluding duplicate cases, two authors conducted the first screening (the first and second MKs) by independently checking the titles and, then, evaluating abstracts. Eligible articles were identified based on a full-text review during the second screening. The references cited in the article that passed the first screening were checked, additional articles were included, and disagreements were resolved through discussion.

Data Extraction

Data were extracted by the first author (MK) and independently checked for accuracy by two other authors (RT and SM). Any disagreement was resolved through discussion.

The following data were extracted: the first author's name, publication year, article type, age, sex, primary disease, use of β-blocker during ECT-induced TCM,

anesthetics, number of ECT before TCM onset, TCM symptoms, clinical course of TCM, ECT retrial, TCM conditions before ECT retrial, duration until ECT retrial, ECT retrial strategies, and TCM recurrence. Cardiogenic shock or abnormal vital signs related to cardiogenic shock are marked with an asterisk in the TCM symptoms section of Table 1. Abnormal vital signs related to cardiogenic shock included hypotension, pulmonary edema, hypoxemia, and pale skin.

Risk-of-Bias Assessment

Two authors (the first and second MKs) assessed the risk of bias in each article using a tool to assess the methodological quality of case reports and case series.[16] This tool included eight items, and two relate to adverse drug event reports, including the challenge or re-challenge phenomenon and a dose-response effect; however, these were inapplicable in this study. Selection bias assessed whether the reported cases were representative of the entire experience of the authors or centers. Assessing selection bias in case reports with respect to specific diseases is not useful except for case control studies or reports of adverse drug events. Therefore, assessing the selection bias of case reports was also considered inapplicable to this review. The five remaining items included exposure ascertainment, outcome ascertainment, accurate diagnosis, follow-up

period, and reporting bias. Each article was judged using a binary (yes or no) response to the items above, and disagreements were resolved through discussion.

Exposure ascertainment assessed the proper description of the conditions; Exposure was defined as ECT. Outcome ascertainment assessed the proper description of outcome; the outcome was defined as TCM development after ECT. Accurate diagnosis assessed the absence of alternative causes that may explain the observation; TCM possesses the diagnostic criteria of the Mayo Clinic or the Japanese Circulation Society. The intact coronary arteries on angiography were essential to diagnosing TCM. However, an alternative method was considered acceptable despite the missing angiography when there were reasons, such as patient refusal of angiography. Follow-up examinations assessed the sufficiency of the surveillance period to detect outcomes; we assessed the description of TCM course and psychiatric diseases after the follow-up. Reporting bias assessed the description of cases with sufficient details to allow for clinical application.

Data Synthesis

Descriptive statistics reported demographic and clinical characteristics as means (standard deviation [SD]) or medians (interquartile range [IQR]) for continuous

variables, and as numbers of cases and frequencies (percentages) for categorical variables. The extracted data are summarized in the tables. Missing values are presented in Table 1 by stating “not described,” and the treatment of missing values is separately presented in the data synthesis results.

RESULTS

The database search yielded 166 articles; after duplicate removal, screening, and citation search, 33 articles describing patients with ECT-induced TCM were identified. Nine articles were excluded due to their provision of only abstracts without the full text, and these excluded articles were Japanese conference reports held in Japan. Finally, 24 articles met the eligibility criteria in this review.[17–40] A PRISMA flow diagram is presented in Figure 1. An article[34] described two ECT-induced TCM cases, while two articles[36,37] described the same patient using different timelines. Consequently, 24 articles/24 cases were selected.

The risk-of-bias assessment of articles is summarized in Figure 2, and the particular risk of bias for each case is presented in Supplemental Digital Content 2. Articles were considered to have a low risk of bias regarding exposure and outcome assessment (24/24 [100%] and 24/24 [100%], respectively), accurate diagnosis (21/24

211 [87.5%]), and reporting bias (24/24 [100%]). Some articles (13/24 [54.2%]) did not
212 include adequate follow-up; therefore, we deemed the articles to have a high risk of bias
213 regarding follow-up.

214 The synthesized characteristics of the 24 ECT-induced TCM cases are
215 presented in Table 1. The 24 articles describing ECT-induced TCM included 13 case
216 reports,[18–21,24,25,27,32,33,35,36,39,40] eight case reports with review,[22,23,26,30,31,34,37,38] and three
217 letter-style case reports.[17,28,29] Most patients were female individuals (21/24 [87.5%]),
218 and the mean (SD) age was 62.3 (15.0) years; Two cases[19,21] were excluded from the
219 analysis because age details were not provided. The primary diseases included 16 cases
220 of major depressive disorders,[19,23–27,29–34,36–40] five cases of bipolar disorder,[17,18,20,34,35]
221 and three cases of schizophrenia.[21,22,28] Eight (33.3%) cases developed ECT-induced
222 TCM despite the use of β-blockers (including bisoprolol,[17,27] metoprolol,[20,26,33,36,37]
223 propranolol,[22,39] and esmolol[26]). One case[26] developed ECT-induced TCM despite the
224 use of intravenous esmolol prior to each ECT session. The anesthetic agents included
225 etomidate (five cases[20,23,24,29,30]), propofol (five cases[17,22,27,30,31]), methohexital (four
226 cases[32,33,36,37,39]), and thiopental or thiamylal (three cases[19,21,40]); eight
227 cases[18,25,26,28,34,35,38] missed the description. Sixteen cases used succinylcholine as a
228 muscle relaxant,[17,19–24,27,29–33,36,37,39,40] and eight missed the description.[18,25,26,28,34,35,38]

Seventeen (70.8%) cases[17,18,21,22,24,27,29,31–40] developed TCM by the third session in the acute ECT course. Ten (41.7%) cases[17,18,21,22,28,29,32,34,39] presented with cardiogenic shock or abnormal vital signs related to cardiogenic shock, and three (12.5%) cases[24,35,40] denied subjective or objective symptoms. All evaluable cases recovered from TCM.

Eight (33.3%) cases[17,20,23,29,30,33,36,37,40] tried to receive ECT retrial after ECT-induced TCM, and their synthesized data are presented in Table 2. The period until ECT retrial was 3 weeks to 9 months; the median (IQR) was 5.5 (4.0–12) weeks. Seven (87.5%) cases[17,20,23,30,33,36,37,40] had ECT re-initiation after TCM wall motion abnormalities had recovered; however, one case[29] had incomplete TCM recovery. All cases took some measures during ECT retrial (including duplicates): Seven cases[17,20,29,30,33,36,37,40] took measures related to β-blockers (dose increase, change, or addition); Three cases[33,36,37,40] for calcium channel blocker addition; one case[23] for change in anesthetic agents; one case for nitrate.[40] ECT could be re-performed without TCM recurrence in all cases. One case[40] experienced a negative T-wave on the ECG after the first ECT re-initiation; however, subsequent ECTs were successful without challenges. This negative T-wave had not been adequately elucidated, and it was unknown if it was a TCM recurrence.

DISCUSSION

We identified 24 cases of ECT-induced TCM, and the patients who developed TCM were predominantly middle-aged and older women, consistent with previously-reported characteristics of TCM.[2,6,41] ECT-induced TCM widely occurred in major depressive disorders, bipolar disorders, and schizophrenia, and there was no specific tendency in the anesthetic agents used. Eight (33.3%) cases developed TCM despite the use of β-blockers, consistent with the previous report, which had observed a certain number of patients who developed TCM, even with β-blockers.[2] Seventeen (70.8%) cases developed TCM by the third session in the acute ECT course, suggesting that ECT-induced TCM develops earlier in the acute course. Ten (41.7%) TCM cases developed cardiogenic shock or abnormal vital signs related to cardiogenic shock, possibly of higher incidence since the frequency of cardiogenic shock in TCM is approximately 10%.[2,42,43] Our results are consistent with those of previous studies reporting that TCMs triggered by perioperative or physical stress are associated with more severe cases than those that were not.[44,45] All evaluable cases were recovered from ECT-induced TCM without severe complications or death.

Nine references of the 33 case reports of ECT-induced TCM were excluded from this review because they had not been described in full text, equivalent to approximately one-fourth of the total. All excluded cases were Japanese reports identified from the Japanese medical literature database, ICHUSHI, and CiNii Research. Perioperative TCM is no longer a novelty and many case reports may have been foregone[46]; The number of ECT-induced TCM cases may be underestimated. Clinicians should be aware of TCM as a complication of ECT.

Avoiding stressors triggering TCM makes sense to prevent recurrence, although preventive measures have not yet been established.[7] However, ECT-induced TCM is problematic with respect to the possibility of patients undergoing ECT multiple times in the future. We observed that eight (33.3%) out of 24 ECT-induced TCM cases tried to be re-challenged with ECT, and they all successfully received ECT retrial without TCM recurrence. ECT was re-initiated after recovery of wall motion abnormalities in most cases, and the period before retrial ECT ranged from 3 weeks to 9 months. The most important result of this report suggests that ECT can be cautiously re-performed after TCM recovery.

Strategies for re-initiating ECT after TCM were inconsistent; nevertheless, measures related to β-blockers were the most prominent, with seven cases identified.

However, the type, dose, and route of administration of β-blockers used varied. The efficacy of β-blockers in preventing TCM remains controversial.[7] β-blockers were previously expected to prevent TCM[47]; however, several reports have revealed no significant effectiveness in using β-blockers for TCM recurrence.[2,48–51] Conversely, there are few reports supporting the efficacy of β-blockers.[52] A prospective randomized study is required to conclude the impact of β-blockers on TCM as previous reports were retrospective or observational studies.

The long-term TCM recurrence rate is approximately 1–11.4%.[2,4,41,48,52–55] The recurrence rate of ECT-induced TCM may not be significant. Nonetheless, patients and clinicians may be reluctant to re-initiate ECT without precautions after it has triggered TCM. The efficacy of β-blockers in preventing TCM is not yet clear, and prophylactic administration of β-blockers during the perioperative period is not approved in Japan. Therefore, we used remifentanil in the ECT retrial, resulting in no TCM recurrence after 10 sessions of the ECT retrial. In addition, remifentanil stabilized hemodynamics during the ECT retrial, as compared with the initial ECT that triggered TCM.

The causes and pathogenesis of TCM are not fully understood. However, catecholamine surge following stress-induced sympathetic stimulation has been viewed as a possible mechanism of cardiotoxicity.[3–6] Stimulation by ECT reportedly releases

300 catecholamines; hence, the suppression of excess catecholamines during ECT may
301 reasonably prevent TCM. Remifentanil significantly inhibits intraoperative
302 catecholamine release[56] and significantly reduces hemodynamic variations during
303 ECT.[57] Opioids have been proposed to effectively prevent perioperative TCM[58];
304 nevertheless, future studies or reports on the prevention of ECT-induced TCM using
305 opioid-based anesthesia are required.

306 In addition to emotional and physical stress, some drugs can trigger TCM due
307 to direct or indirect catecholamine stimulation. Kido et al. identified 157 cases of drug-
308 induced TCM in their systematic literature search.[59] Regarding medications associated
309 with psychiatric disorders, lithium and serotonin norepinephrine reuptake inhibitors
310 (SNRIs) have been reported as causative agents of TCM.[59-61] Whereas there is some
311 evidence that rapid uptitration or overdose of SNRIs may induce TCM, there are no
312 similar reports on noradrenergic and specific serotonergic antidepressants (NaSSAs).
313 There is one report of a patient with post-traumatic stress disorder with repeated TCM
314 who was treated with mirtazapine (NaSSA) to avoid SNRIs.[62] Selective serotonin
315 reuptake inhibitors (SSRIs) are considered relatively safe for populations with
316 cardiovascular vulnerability[63], however, only fluoxetine may be related to the
317 development of TCM by increasing the norepinephrine levels.[64] When our patient

developed ECT-induced TCM, the medications included lurasidone, escitalopram (SSRI), and mirtazapine (NaSSA). When ECT was reinitiated, medications included sertraline (SSRI) and olanzapine. Lurasidone and olanzapine are both atypical antipsychotics with α adrenergic antagonism, although they differ in affinity and selectivity.[65] To date, there is no evidence concerning whether atypical antipsychotics influence the development of TCM.

This report has some limitations. First, the case report included only one case; therefore, the generalized application of the results is limited. The ECT retrial was successfully performed with simultaneous remifentanil use without TCM recurrence; however, the significant effect of remifentanil remains unverified. This systematic review summarized previously reported cases, and we included 24 case reports, eight of which re-performed ECT, which is insufficient to discuss the TCM recurrence rate. Studies with more evidence, such as randomized controlled trials and prospective observational studies, could not be identified. Furthermore, language restrictions were not set for this review; however, keywords were searched for in English and Japanese, and more cases could have been revealed by searching in other languages. Case reports possess some inherent bias, including detection, publication, and information bias, and more severe and successful cases may be reported. Furthermore, the articles included in

our review had a high risk of bias regarding follow-up. TCM was first described in Japan in 1990 and has subsequently become a globally recognized disease.[1, 2, 66] Therefore, the search period was set from 1990 onward. TCM likely existed prior to 1990; however, earlier reports were not included in this review.

In conclusion, clinicians should be aware of TCM as a complication of ECT. ECT-induced TCM is more likely to cause life-threatening cardiogenic shock than non-perioperative cases; nevertheless, it has good prognosis. ECT can be cautiously reinitiated after TCM recovery; however, preventive measures for TCM are currently controversial. In our case, remifentanil was used in the ECT retrial, resulting in no TCM recurrence. Further studies are required to determine preventive measures for ECT-induced TCM.

ACKNOWLEDGEMENTS

The authors thank Editage (www.editage.com) for English language editing.

AUTHOR CONTRIBUTIONS

Michiko Kinoshita wrote the draft, managed the anesthesia, obtained the patient's consent, collected/interpreted the literature, and performed data analysis. Makoto

Kinoshita managed the psychiatric treatment, collected/interpreted the literature, performed data analysis, and edited the manuscript. Rikako Takahashi performed data analysis, helped in interpreting the literature, and edited the manuscript. Sarara Mutoh performed data analysis, helped in interpreting the literature, and edited the manuscript. Nami Kakuta supervised the anesthetic management, helped in interpreting the literature, and edited the manuscript. Katsuya Tanaka supervised the anesthetic management, helped in conceiving/designing the study, helped in interpreting the literature, and edited the manuscript. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST AND SOURCE OF FUNDING

Non declared

366 **FIGURE LEGENDS**

367 **FIGURE 1.** PRISMA flow diagram.

368 n, number; TCM, takotsubo cardiomyopathy; ECT, electroconvulsive therapy

369

370 **FIGURE 2.** The risk-of-bias assessment.

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Table 1: The characteristics of ECT-induced TCM

1st Author (Ref. No.)	Year	Sex	Age	Primary Disease	β-blockers use during ECT that induced TCM	Anesthesia	Previous ECT before TCM onset (session/course)*1	TCM Symptoms	TCM Course
Guine[17]	2022	F	69	BD	Bisoprolol	Propofol, succinylcholine	2/3rd course	Acute respiratory failure, cardiogenic shock*5	Improved
Miyahara[18]	2020	F	67	BD	ND	ND	2/1st course	Hypotension*5	Improved
Sasaki[19]	2019	F	50's	MD	ND	Thiopental, succinylcholine	4/1st course	Ventricular Tachycardia	Improved
Clifford[20]	2019	F	65	BD	Metoprolol	Etomidate, succinylcholine	26th session (maintenance ECT)	Brief apneic, syncope	Improved
Seto[21]	2018	F	60's	SC	ND	Thiamylal, succinylcholine	2/1st course	Cardiogenic shock*5	Improved
Medved[22]	2018	M	40	SC	Propranolol	Propofol, succinylcholine	1/1st course	Gastric pain, pale, tachypneic without a palpable radial pulse, shortness of breath*5	Improved

Kudling[23]	2018	M	63	MD	ND	Etomidate, succinylcholine, atracurium	11/2nd course	Chest discomfort, hyper tension	Improved
Krause[24]	2015	F	50	MD	ND	Etomidate, succinylcholine	2/1st course	No symptom	Improved
De Wolf[25]	2015	F	67	MD	ND	ND	24th session (maintenance ECT)	Chest pain	Improved
Agarwal[26]	2015	F	67	MD	Oral metoprolol, intravenous esmolol	ND	6/1st course*2	Sinus tachycardia	Improved
Narayanan[27]	2014	F	74	MD	Bisoprolol	Propofol, succinylcholine	1/2nd course	Acute epigastric discomfort	Improved
Grubisha[28]	2014	M	31	SC	ND	ND	The final session (> 50 ECT)	Hypotension*5	Improved
Binhas[29]	2013	F	85	MD	ND	Etomidate, succinylcholine	3/unknown course	Dyspnea, hypoxemia*5	Improved
Celano[30]	2011	F	76	MD	ND	Etomidate, propofol, succinylcholine	11th session (1st maintenance ECT after 10 acute ECT)	Chest pain radiating to back	Improved

Serby[31]	2010	F	90	MD	ND	Propofol, succinylcholine	3/ unknown course (> 100 ECT)	ND	Improved
Beach[32]	2010	F	52	MD	ND	Methohexital, succinylcholine	1/1st course*2	Chest pain, nausea, jaw pain, hypotension*5	Improved
Kent[33]	2009	F	71	MD	Metoprolol	Methohexital, succinylcholine	3/2nd course *3	Chest tightness	Improved
Go[34]	2009	F	50	MD	ND	ND	3/1st course*2	Dyspnea, hypoxemia, moderate pulmonary edema*5	Improved
Go[34]	2009	F	49	BD	ND	ND	1/1st course*2	Tachycardia, dyspnea, hypotension*5	Improved
Chandra[35]	2009	F	70	BD	ND	ND	1/1st course*2	No symptom	Improved
Littlejohn[36]	2008	F	71	MD	Metoprolol	Methohexital, succinylcholine	1/2nd course	Chest pain, dyspnea	Improved
Satterthwaite[37] *4	2009		72						
O'Reardon[38]	2008	F	45	MD	ND	ND	3/1st course	Non-radiating, substernal chest pain, hypertension, tachycardia	Improved
Ring[39]	1996	F	41	MD	Propranolol	Methohexital, succinylcholine	1/1st course*2	Pinky frothy fluid, hypoxemia*5	Improved
Zhu[40]	1992	F	77	MD	ND	Thiopental, succinylcholine	1/1st course*2	No symptom	Improved

Ref. No., reference number; ECT, electroconvulsive therapy; TCM, takotsubo cardiomyopathy; MD, Major depression; BD, Bipolar disorder; SC, Schizophrenia; ND, not described.

**1: In cases of acute ECT, session/course was listed; otherwise, the number of times was noted.*

**2: Judged based on the text, though not clearly described.*

**3: The two initial sessions were below the convulsive threshold.*

**4: Two articles described the same patient in different time series.*

**5: Cardiogenic shock or abnormal vial signs related to cardiogenic shock.*

Table 2: The data of retrial ECT after ECT-induced TCM

1st Author (Ref. No.)	Year	Condition of TCM before retrial ECT	Duration to retrial ECT	Management for ECT retrial	TCM recurrence
Guine[17]	2022	Improved	4 weeks	Change in β-blocker Bisoprolol→atenolol	No
Clifford[20]	2019	Improved	4 weeks	Increased dose of metoprolol, Addition of esmolol	No
Kudling[23]	2018	Improved	5 weeks	Change in anesthetic agents Etomidate→methohexital	No
Binhas[29]	2013	Not yet improved	3 weeks	Addition of bisoprolol	No
Celano[30]	2011	Improved	1.5 months	Addition of intravenous labetalol	No
Kent[33]	2009	Improved	2 months	Addition of intravenous esmolol and nicardipine	No
Littlejohn[36] Satterthwaite[37]	2008 2009	Improved	9 months	Addition of labetalol or esmolol, and nicardipine	No
Zhu[40]	1992	Improved	6 months	Addition of nitrates, diltiazem and labetalol*1	Yes/No*2

Ref. No., reference number; ECT, electroconvulsive therapy; TCM, takotsubo cardiomyopathy.

**1: Nitrate and diltiazem were used in the first ECT retrial; Labetalol was used in the second ECT retrial.*

**2: This case developed a negative T-wave on electrocardiogram after the first ECT retrial; however, no recurrence on the subsequent retrial ECT was observed.*

Figure 1

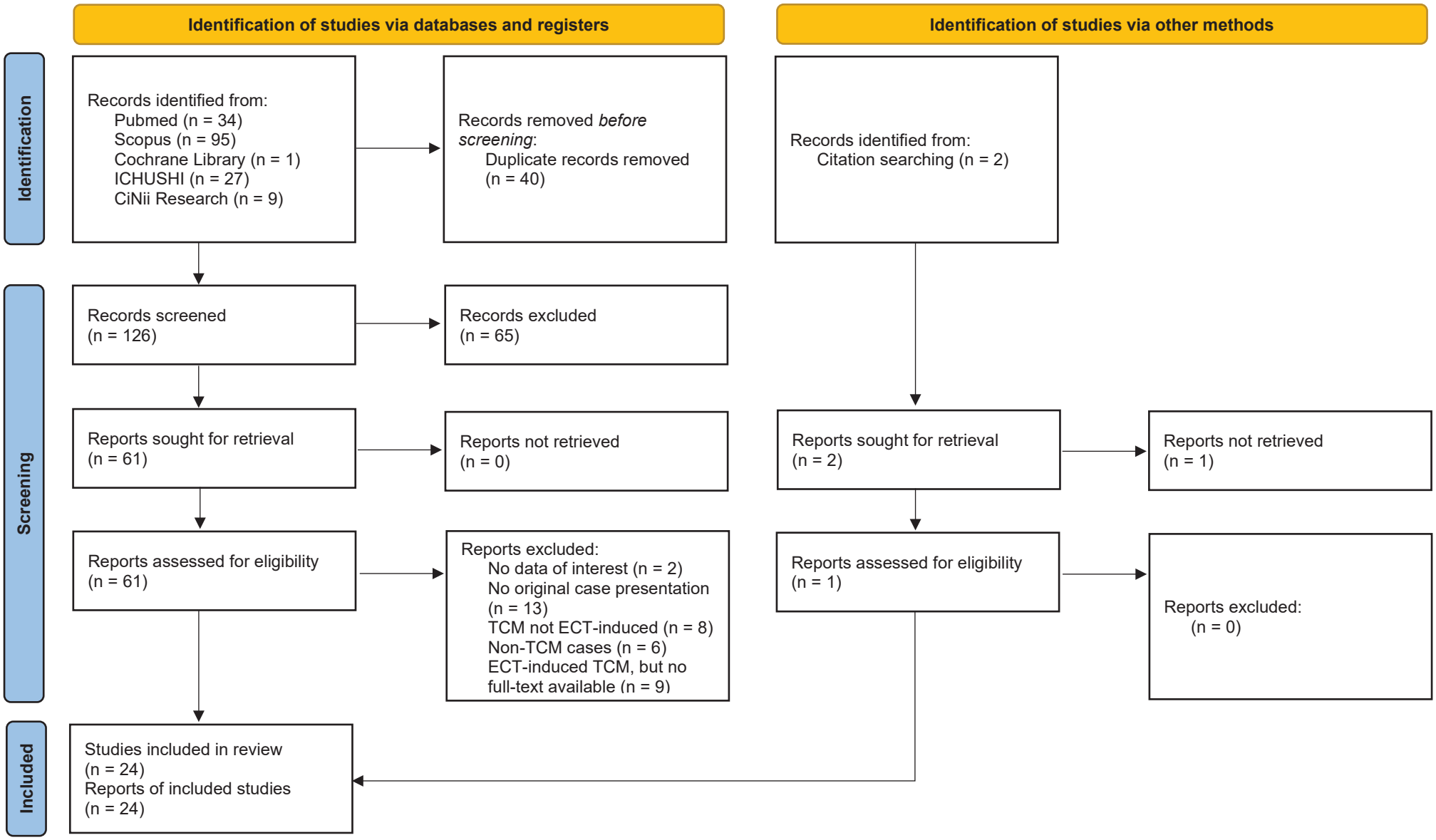
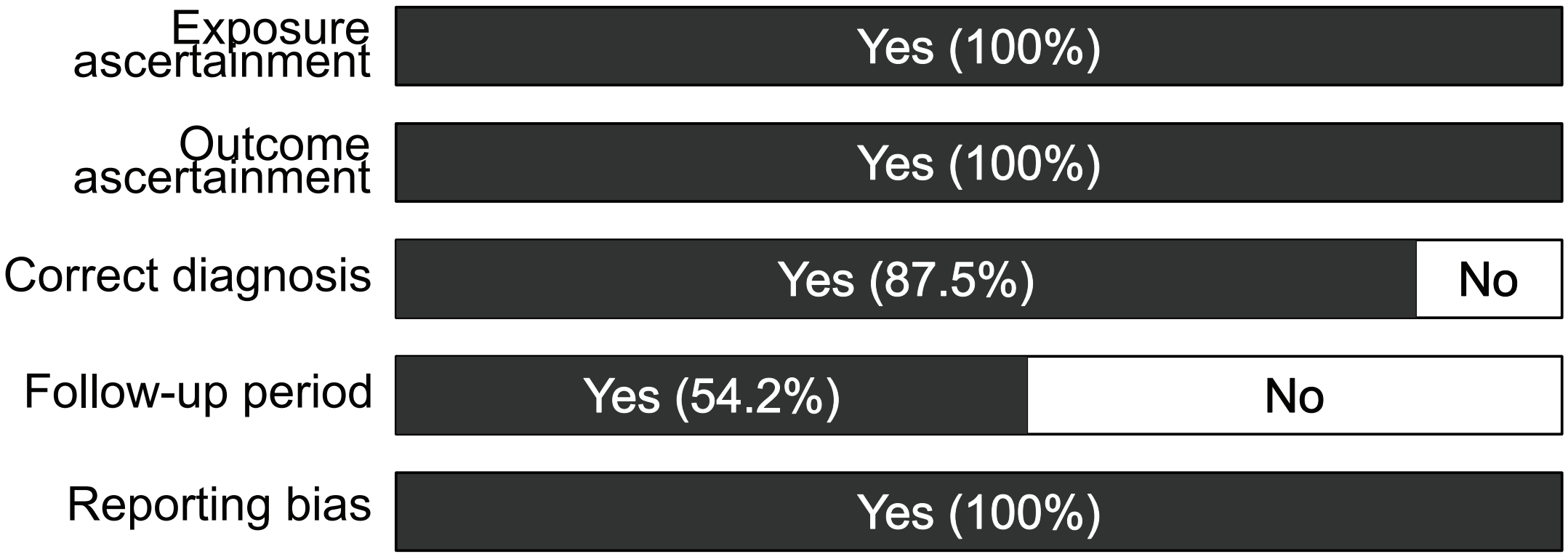

Identification of studies via databases and registers
Identification of studies via other methods
Identification
Screening
Included
Records identified from:
Pubmed (n = 34)
Scopus (n = 95)
Cochrane Library (n = 1)
ICHUSHI (n = 27)
CiNii Research (n = 9)
Records removed *before screening*:
Duplicate records removed (n = 40)
Records identified from:
Citation searching (n = 2)
Records screened (n = 126)
Records excluded (n = 65)
Reports sought for retrieval (n = 61)
Reports not retrieved (n = 0)
Reports sought for retrieval (n = 2)
Reports not retrieved (n = 1)
Reports assessed for eligibility (n = 61)
Reports excluded:
No data of interest (n = 2)
No original case presentation (n = 13)
TCM not ECT-induced (n = 8)
Non-TCM cases (n = 6)
ECT-induced TCM, but no full-text available (n = 9)
Reports assessed for eligibility (n = 1)
Reports excluded: (n = 0)
Studies included in review (n = 24)
Reports of included studies (n = 24)

Figure 2


Exposure ascertainment
Yes (100%)
Outcome ascertainment
Yes (100%)
Correct diagnosis
Yes (87.5%)
No
Follow-up period
Yes (54.2%)
No
Reporting bias
Yes (100%)

The Safety and Strategies for Reinitiating Electroconvulsive Therapy (ECT) After ECT-induced Takotsubo Cardiomyopathy: A Case Report and Systematic Review

Michiko Kinoshita, M.D., Ph.D.[1], Makoto Kinoshita, M.D., Ph.D.[2], Rikako Takahashi, M.D.[1], Sarara Mutoh, M.D.[1], Nami Kakuta, M.D., Ph.D.[1], and Katsuya Tanaka, M.D., Ph.D.[1]

[1] Department of Anesthesiology, Tokushima University Hospital, 2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan
[2] Department of Psychiatry, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-8-15 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan

Corresponding Author: Michiko Kinoshita
2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan
Telephone number: +81 (0)88-633-7181, Fax number: +81 (0)88-633-7182
Email: michiko-kinoshita@tokushima-u.ac.jp

Supplemental Digital Content 1: Research strategy

MEDLINE (pubmed)

("Electroconvulsive Therapy"[MeSH Terms] OR ("electroconvulsant"[All Fields] OR "electroconvulsion"[All Fields] OR "electroconvulsions"[All Fields] OR "electroconvulsive"[All Fields]) OR ("electroshock"[MeSH Terms] OR "electroshock"[All Fields] OR "electroshocks"[All Fields]) OR "electric shock"[All Fields] OR "ect"[All Fields]) AND ("Takotsubo Cardiomyopathy"[MeSH Terms] OR ("takotsubo"[All Fields] OR "takotsubo s"[All Fields]) OR "tako-tsubo"[All Fields] OR "Takotsubo Cardiomyopathy"[All Fields] OR "tako-tsubo cardiomyopathy"[All Fields] OR "stress cardiomyopathy"[All Fields] OR "stress-induced cardiomyopathy"[All Fields] OR "stress-induced cardiomyopathy"[All Fields] OR "ampulla cardiomyopathy"[All Fields] OR "catecholamine cardiomyopathy"[All Fields] OR "catecholamine-induced cardiomyopathy"[All Fields] OR "catecholamine cardiotoxicity"[All Fields] OR "catecholamine-induced cardiotoxicity"[All Fields] OR "catecholamine-induced cardiotoxicity"[All Fields] OR "broken heart"[All Fields] OR "apical ballooning"[All Fields] OR "ventricular ballooning"[All Fields] OR "transient regional left ventricular dysfunction"[All Fields] OR "transient myocardial dysfunction"[All Fields] OR "transient systolic dysfunction"[All Fields] OR "stunned myocardium"[All Fields] OR "myocardial stunning"[All Fields] OR "neurocardiogenic stunning"[All Fields] OR "cardiogenic shock"[All Fields] OR (("neurogenic"[All Fields] OR "neurogenically"[All Fields] OR "neurogenics"[All Fields]) AND ("stress"[All Fields] OR "stressed"[All Fields] OR "stresses"[All Fields] OR "stressful"[All Fields] OR "stressfulness"[All Fields] OR "stressing"[All Fields]) AND ("myocardium"[MeSH Terms] OR "myocardium"[All Fields] OR "myocardiums"[All Fields])) OR "reversible acute heart failure"[All Fields])

Scopus

(electroconvulsive OR electroshock OR "electric shock" OR “ect”) AND (takotsubo OR tako-tsubo OR “takotsubo cardiomyopathy” OR “tako-tsubo cardiomyopathy” OR “stress cardiomyopathy” OR “stress induced cardiomyopathy” OR “stress-induced

cardiomyopathy” OR “ampulla cardiomyopathy” OR “catecholamine cardiomyopathy” OR “catecholamine-induced cardiomyopathy” OR “catecholamine cardiotoxicity” OR "catecholamine induced cardiotoxicity" OR "catecholamine-induced cardiotoxicity" OR "broken heart" OR "apical ballooning" OR "ventricular ballooning" OR “transient regional left ventricular dysfunction” OR “transient myocardial dysfunction” OR “transient systolic dysfunction” OR “stunned myocardium” OR “myocardial stunning” OR “neurocardiogenic stunning” OR “cardiogenic shock” OR “neurogenic stressed myocardium” OR “reversible acute heart failure”)

Cochrane Library

(electroconvulsive OR electroshock OR "electric shock" OR “ect”) AND (takotsubo OR tako-tsubo OR “takotsubo cardiomyopathy” OR “tako-tsubo cardiomyopathy” OR “stress cardiomyopathy” OR “stress induced cardiomyopathy” OR “stress-induced cardiomyopathy” OR “ampulla cardiomyopathy” OR “catecholamine cardiomyopathy” OR “catecholamine-induced cardiomyopathy” OR “catecholamine cardiotoxicity” OR "catecholamine induced cardiotoxicity" OR "catecholamine-induced cardiotoxicity" OR "broken heart" OR "apical ballooning" OR "ventricular ballooning" OR “transient regional left ventricular dysfunction” OR “transient myocardial dysfunction” OR “transient systolic dysfunction” OR “stunned myocardium” OR “myocardial stunning” OR “neurocardiogenic stunning” OR “cardiogenic shock” OR “neurogenic stressed myocardium” OR “reversible acute heart failure”)

ICHUSHI (in Japanese)

(電気ショック/TH or 電気けいれん療法/TH) and (心筋症-たこつぼ型/TH or (心筋疾患/TH or 心筋症/AL))

CiNii (in Japanese)

(電気痙攣 OR 電気けいれん OR 電気ショック) AND (たこつぼ OR 心筋症)

(electroconvulsive OR electroshock OR "electric shock" OR “ect”) AND (takotsubo OR tako-tsubo OR “takotsubo cardiomyopathy” OR “tako-tsubo cardiomyopathy” OR

“stress cardiomyopathy” OR “stress induced cardiomyopathy” OR “stress-induced cardiomyopathy” OR “ampulla cardiomyopathy” OR “catecholamine cardiomyopathy” OR “catecholamine-induced cardiomyopathy” OR “catecholamine cardiotoxicity” OR "catecholamine induced cardiotoxicity" OR "catecholamine-induced cardiotoxicity" OR "broken heart" OR "apical ballooning" OR "ventricular ballooning" OR “transient regional left ventricular dysfunction” OR “transient myocardial dysfunction” OR “transient systolic dysfunction” OR “stunned myocardium” OR “myocardial stunning” OR “neurocardiogenic stunning” OR “cardiogenic shock” OR “neurogenic stressed myocardium” OR “reversible acute heart failure”)

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[1] Department of Anesthesiology, Tokushima University Hospital, 2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan
[2] Department of Psychiatry, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-8-15 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan

Corresponding Author: Michiko Kinoshita
2-50-1 Kuramoto-cho, Tokushima-shi, Tokushima 770-8503, Japan
Telephone number: +81 (0)88-633-7181, Fax number: +81 (0)88-633-7182
Email: michiko-kinoshita@tokushima-u.ac.jp

Supplemental Digital Content 2: The risk bias assessment of each case

1st Author (Rf. No.)	Exposure assessment	Outcome assessment	Correct diagnosis	Follow-up period	Reporting bias
Guine[17]	Yes	Yes	Yes	Yes	Yes
Miyahara[18]	Yes	Yes	Yes	Yes	Yes
Sasaki[19]	Yes	Yes	Yes	Yes	Yes
Clifford[20]	Yes	Yes	Yes	Yes	Yes
Seto[21]	Yes	Yes	No	No	Yes
Medved[22]	Yes	Yes	Yes	No	Yes
Kudling[23]	Yes	Yes	Yes	Yes	Yes
Krause[24]	Yes	Yes	Yes	No	Yes
De Wolf[25]	Yes	Yes	Yes	Yes	Yes
Agarwal[26]	Yes	Yes	Yes	No	Yes
Narayanan[27]	Yes	Yes	Yes	Yes	Yes
Grubisha[28]	Yes	Yes	Yes	No	Yes
Binhas[29]	Yes	Yes	Yes	No	Yes
Celano[30]	Yes	Yes	Yes	Yes	Yes
Serby[31]	Yes	Yes	Yes	Yes	Yes
Beach[32]	Yes	Yes	Yes	Yes	Yes
Kent[33]	Yes	Yes	Yes	Yes	Yes
Go[34]	Yes	Yes	No	No	Yes
Go[34]	Yes	Yes	No	No	Yes
Chandra[35]	Yes	Yes	Yes	No	Yes
Littlejohn[36]	Yes	Yes	Yes	Yes	Yes
Satterthwaite[37] *4					
O'Reardon[38]	Yes	Yes	Yes	Yes	Yes
Ring[39]	Yes	Yes	Yes	No	Yes
Zhu[40]	Yes	Yes	Yes	No	Yes

Ref. No., reference number; ND, not described.

**1: Two articles described the same patient in different time series.*