


Integrated cognitive behavioral therapy for chronic pain

An open-labeled prospective single-arm trial

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Abstract

Background: We aimed to examine the feasibility of our newly developed, integrated, and high-intensity individual cognitive behavioral therapy (CBT) protocol for treatment-resistant chronic pain.

Methods: We conducted an open-labeled prospective single-arm trial for patients aged 18 years and above, suffering from chronic pain, and diagnosed with somatic symptom disorder with predominant pain. We provided 16 weekly sessions of CBT, each lasting for 50 minutes, which included 4 new strategies: attention shift, memory work, mental practice, and video feedback. For comparison, the study had a pre-test post-test design. The primary outcome was the change from baseline (week 1) to 16, as indicated by the Numerical Rating Scale and Pain Catastrophizing Scale. In addition, we evaluated depression, anxiety, disability, and quality of life as secondary outcomes.

Results: Sixteen patients with chronic pain underwent our CBT program. Though there was no reduction in pain intensity, catastrophic cognition showed statistically significant improvement with a large effect size. Depression, anxiety, and disability demonstrated statistically significant improvements, with small to moderate effect sizes. No adverse events were reported.

Conclusion: Our newly integrated CBT program for chronic pain may improve catastrophic cognition, depression, anxiety, and disability. Large-scale randomized controlled studies are necessary to investigate the program's effectiveness in the future.

Abbreviations: CBT = cognitive behavioral therapy, DSM-5 = diagnostic and statistical manual of mental disorders fifth edition, EQ-5D-5L = EuroQOL 5 dimensions 5-level, GAD-7 = generalized anxiety disorder scale, NRS = numerical rating scale, PCS = pain catastrophizing scale, PDAS = pain disability assessment scale, PHQ-9 = patient health questionnaire-9.

Keywords: chronic pain, individual cognitive behavioral therapy, memory work, somatic symptom disorder, visual image

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1. Introduction

1.1. Background

Chronic pain is highly prevalent worldwide, and it poses a substantial financial, occupational, psychological, and social burden. In the World Health Organization's International Classification of Diseases International Disease Classification Version 11, chronic pain is divided into 7 groups.^[1] One of them, chronic primary pain, is defined as persisting or recurring pain for longer than 3 months; being associated with significant emotional distress (e.g., anxiety, anger, frustration, or depressed mood) and/or significant functional disability (interference in activities of daily life and participation in social roles); and having symptoms that are not better accounted for by another diagnosis.^[2] This definition of chronic primary pain aims to avoid the obsolete dichotomy of "physical" vs. "psychological".^[3] Similarly, in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), "somatic symptom disorder with predominant pain" replaces DSM-IV's "pain disorder". Katz et al^[4] do not recommend the diagnostic name for patients with chronic pain, because the term lacks validity and overpsychologizes patients.

Cognitive behavioral therapy (CBT) uses a biopsychosocial approach for treatment and can be used in a multidisciplinary pain management program. CBT, which encourages patients to take control of their pain problem and lead a fulfilling life in spite

of the pain, should be offered in pain clinics^[5]; however, CBT is offered in about 35% of Japan's clinics.^[6] CBT, which can directly intervene in excessive ideas, concerns, emotions, and behaviors related to physical symptoms, is the most common psychological treatment for chronic pain. It has been shown to be effective by systematic reviews and meta-analyses based on many clinical trials.^[7–10] The latest systematic review of 75 randomized controlled trials (n=9401), on the effectiveness of face to face CBT has shown that CBT versus treatment-as-usual to end pain, disability and distress showed a small effect size, and versus active treatment showed few effects.^[10]

There are a lot of CBT strategies which were effective, however some of them are insufficient still. Most CBT strategies, comprising 8 to 12 sessions and each lasting 30 to 50 minutes, include psychoeducation, relaxation, cognitive restructuring, stress management, activity pacing, behavioral activation, anger control, and relapse prevention^[11,12]. There are no studies verifying the effectiveness of CBT strategies, and it is not known which combination and/or duration of these sessions are more effective.

We think some improvement in CBT strategies for chronic pain is needed. For that, clinical data should be accumulated of new strategies, actively trying novel combinations of the strategies, and adjusting the duration of the interventions.

1.2. Aim of study

We aimed to examine the effectiveness and feasibility of our integrated and high-intensity individual CBT protocol for treatment-resistant chronic pain. To do that, first, we developed 16 weekly 50-minute sessions of CBT protocol, including 4 new strategies. Second, we designed an open-labeled prospective single-arm trial for patients aged 18 years and above, suffering from chronic pain. Third, we verified the effectiveness of the program by pain intensity, catastrophic cognition, etc.

2. Methods

2.1. Study design

This interventional study was designed as a prospective, open-labeled, single-arm trial. In the 1-group pretest–post-test design, a pre-intervention evaluation was performed in CBT session 1 and a post-intervention evaluation in session 16. The study was conducted at the academic outpatient clinic of the CBT Center in Chiba University Hospital.

2.2. Participants and recruitment

Patients with chronic pain were recruited through posters and leaflets placed at medical institutions in Chiba Prefecture and through web-based and newspaper advertisements from April 2017 to April 2019. This study was also announced for the outpatients in the Department of Orthopedics and Pain Anesthesiology in the Chiba University Hospital. All patients continued treatment as usual, including pharmacotherapy with their primary care physician after obtaining their physician's permission prior to enrollment. Each patient's treatment history was confirmed by their prescribing clinician and by chart review. All patients were evaluated by 2 researchers (E.S., who is a psychiatrist and K.T., who is a therapist). The researchers also confirmed the patient diagnosis and eligibility and discussed the validity of the patient's initial diagnosis and eligibility.

2.3. Inclusion and exclusion criteria

Patients were required to meet the following inclusion criteria for participation: aged 18 years or above; having a primary diagnosis of somatic symptom disorder with predominant pain according to the DSM-5; and having at least moderate-intensity chronic pain despite receiving pharmacotherapy, including antidepressants, having at least moderate-intensity chronic pain despite receiving pharmacotherapy, including antidepressants, for 8 weeks. The exclusion criteria included presence of severe mental disorders (neurocognitive, psychotic, bipolar, and substance disorders), developmental disorders, and mental retardation. Patients with Pain Disability Assessment Scale (PDAS) score less than 10 despite undergoing pharmacotherapy were also excluded.

2.4. Intervention

The intervention in this study comprised a 50-minute CBT session once a week for 16 consecutive weeks. Patients received assessment sessions with their therapists and then started weekly face to face CBT. In each session, patients and therapists used the same workbook of the integrated CBT, and patients were encouraged to write down important information and homework.

2.5. Integrated CBT for chronic pain

Based on our previous studies to develop our new CBT program for panic disorder^[13–15] and for major depressive disorder^[16,17] based on the Clark and Wells model for social anxiety disorder,^[18–20] we incorporated the following 4 sessions that have not been used in CBT protocols for chronic pain (Table 1).

2.5.1. Tactile attention-shift training (session 4). Patients with chronic pain tend to subconsciously pay excessive attention to the painful area. They need to recognize and correct their attention bias to pain. Visual and auditory attention shift is a general exercise in CBT for anxiety disorders. We apply tactile attention shifting technique for patients with chronic pain. Meanwhile, the therapeutic effect of “touch” to relieve pain has been reported,^[21] and tactile care has been established as a professional, noninvasive approach for lower back pain.^[22] Tactile care is based on the hypothesis that pain can be relieved through promoting secretion of oxytocin through the therapist's gentle touch on the affected body part. By combining attention shift with tactile self-pare, patients can be encouraged to practice attention shifting by self-touch. First, the therapist informs the patient that individuals can flexibly shift their attention after the training. Second, patients are asked to pay attention to their painful body part, touch that part with their own hands, and verbally explain their tactile senses. Third, patients are asked to touch a painless body part and pay attention to the tactile senses. Fourth, patients are asked to shift their attention from the body part without pain to the body part with pain and repeat the sequence.

2.5.2. Memory work using the peak-end rule (session 10).

Treating intrusive images using imagery rescripting of CBT has been reported for a variety of mental disorders including posttraumatic stress disorder, anxiety disorders, depression, nightmares, and personality disorders. In imagery rescripting, the patient imagines the traumatic experience and then imagines an

Table 1
Integrated cognitive behavioral therapy protocol for chronic pain.

Integrated CBT protocol for chronic pain		
Session 1	Introduction	Therapists explained the purpose of CBT and set short, medium, and long term treatment goals.
Session 2	Psychoeducation	Patients studied ideas such as mechanism of pain, gate-control theory, and acceptance of pain.
Session 3	Relaxation	Patients practiced progressive muscle relaxation and abdominal breathing techniques.
Session 4	Tactile attention-shift training	Patients practiced shifting their excessive attention of pain flexible.
Session 5	Case formulation	Patients learned their own cognitive behavioral models and vicious pain-causing cycles.
Session 6	Safety behaviors	For behavioral activation, patients understand avoiding action due to pain and to learn the demerits of continuing safety action such as avoid, makeshift action.
Session 7	Cognitive restructuring 1	Examining patients' thinking habits and learning how to change their irrational thinking.
Session 8	Cognitive restructuring 2	
Session 9	Activity pacing	Spacing out activities to manage pain
Session 10	Memory work using the peak end rule.	By re-examining patients' pain memory, patients learn that their pain memory influences chronic pain.
Session 11	Mental practice	Patients practice imagining the movement of their body that is in pain and maintain hope.
Session 12	Visual feedback	Performing mirror therapy as an alternative, recording patients' own actions, and observing ideal movement.
Session 13	Behavioral experiments 1	Practicing step by step actions which could not be performed because of pain.
Session 14	Behavioral experiments 2	
Session 15	Summary	Review the entire session and confirm whether there are any remaining issues.
Session 16	Relapse prevention	Thinking about how to respond when the pain recurs.

CBT = cognitive behavioral therapy.

intervention that changes the course of events so that a more satisfying outcome is achieved.^[23] We attempted to apply imagery rescripting to CBT for chronic pain.

In this session, we aimed to do an imagery rescripting for patients' traumatic pain memory. Most patients with chronic pain are overwhelmed by intense and painful memories. Usually patients have had a past experience of pain that was stronger than their present pain; their painful memory is traumatic in itself. Fredrickson and Kahneman^[24] showed that unpleasant experiences such as pain are memorized as the average of the peak pain and the end pain, with the moment experienced as the most painful being the "peak" and the moment the pain reduced being the "end". According to the peak-end rule, patients with chronic pain remember the peak pain as being so intense they could not recognize very clearly when the pain was alleviated at the end of the experience, and thus they are unable to form a positive memory. Therefore, their average rating of the pain tends to be high, and the experience is deemed as intense. In our intervention sessions, we expected that patients would be able to recognize that their pain would be alleviated by detailing the memory of their painful episode from start to finish and rescripting their memory to make it reversible and temporal for a longer time.

2.5.3. Mental practice of action using motor imagery rescripting (session 11). Motor imagery is considered effective for learning and practicing movements in many fields.^[25] Mental practice of action using motor imagery is performed in post-stroke rehabilitation and sports science. This technique is forms part of psychological skills training that supports physical or rehabilitative practice, the goal normally being to enhance or maintain performance of a skill or task.^[26–28] Patients with chronic pain tend to show a conditioned response to motor imagery and strongly believe that they should not move their painful body part, because rest is the most important. To change the catastrophic misinterpretation of body sensations, patients during this session try to imagine that they can move their body parts without pain. They practice clear visualization of painless movement of the body parts by creating a short daily routine story. During the mental practice, patients do not move their

painful body part. Through repeated mental practice by motor image exercise, there is a possibility of improving their movement without physical burden.^[29] Even without real-time video feedback, imagining repeated movements of their painful body part may lead to behavioral activation.^[30]

2.5.4. Video feedback including mirror therapy (session 12). In mirror therapy, used as treatment for phantom limb pain,^[31] patients observed movement of their healthy side as reflected in a mirror. Through this visual recognition, the brain interprets that the amputated side is moving, and the pain is alleviated.^[32,33] If chronic pain is regarded as a state in which senses and motor contact to the brain are severely disconnected, as with phantom limb pain, it is expected that the pain will be alleviated by continuing to observe the image of the patient's own painful body part moving. Regarding mirror therapy for chronic pain, although it is easy to view the limb in a mirror, it is difficult to view the head, neck, or trunk in a mirror. Video feedback is an effective component of CBT^[34] for social anxiety disorder, and from our previous clinical study, our therapists are experienced at providing CBT video feedback. Video feedback is effective not only in mirror therapy but also to alleviate pain. In a previous study, patients with chronic back pain received a real-time video feedback of their own back during a conventional massage therapy, and the effect of visually induced analgesia was observed.^[35] Instead of mirror therapy, we use videotape feedback to restructure dysfunctional motor imagery with pain into functional motor imagery without pain. In this session, patients viewed video recordings of another person's movement of their body parts without pain—which the patient did not want to or could not move due to chronic pain—as if they were doing it by themselves.

2.6. CBT therapist and quality control

The CBT was provided by 8 trained therapists including 1 doctor, 1 nurse, 4 clinical psychologists, and 2 mental health care workers. All therapists had completed a 2-year high intensity CBT training course known as the Chiba Improving Access to

Psychological Therapies Project: Chiba-IAPT.^[36] The therapists recorded all sessions during the intervention period and managed the quality of CBT through supervision at appropriate intervals.

2.7. Ethics and dissemination

This study was conducted under the approval of the Institutional Review Board of Chiba University Hospital (approval ID number: G28049). In addition, the Clinical Research Ethics Review Committee was examined at least annually to determine if this test was properly implemented. The trial registration number was UMIN000027153.

Those who wished to participate in the study were informed of its purpose, after which they confirmed their willingness to participate in the first interview. Each patient was notified that participation was voluntary and complete anonymity was provided. They were asked to provide written informed consent. An adverse event could consist of any unfavorable and unintended sign, symptom, or disease temporarily associated with this interventional study, regardless of its relation to the intervention of this study. All adverse events were reported, and serious adverse events were immediately reported to the Institutional Review Board of Chiba University Hospital in addition to being registered with the hospital risk management system.

2.8. Outcome measures

Baseline characteristics of patients including gender, age, education, marital status, employment status, age at the onset of chronic pain, and duration of chronic pain were assessed. The following assessment items were set based on initiative on methods measurement and pain assessment in clinical trials “Assessment of Chronic Pain” recommended by the International Pain Society.^[37]

2.9. Primary outcomes

The primary outcome was the change from baseline (week 1) to 16 as indicated by the Numerical Rating Scale (NRS) and Pain Catastrophizing Scale (PCS) scores. NRS is a self-rated questionnaire to measure pain intensity on a 0 to 10 scale (0= nothing–10=severe). Patients maintained a pain diary to record subjective pain intensity every day. The average of the maximum and minimum pain was recorded as a daily pain score, and the final NRS score at the end of the week was calculated as the average of daily pain scores per week (sum of 7 days’ NRS scores divided by 7). The PCS comprises 13 items that evaluate the degree of patients’ catastrophic cognition about pain. The responses are recorded on a 5-point scale from (0) not at all to (4) all the time. The total PCS scores range from 0 to 52 and the clinical cutoff value for the score is over 30.^[38]

2.10. Secondary outcomes

In addition to primary outcomes from baseline to week 16, NRS and PCS changes from baseline to week 8, and changes from baseline to week 8 and 16 were analyzed as secondary outcomes.

Degree of daily life impairment because of pain was measured with the PDAS, which consists of 20 items, and the degree of life disability was evaluated on a 4-point Likert-scale. It evaluated from 0 to 60 points, and the higher the score, the higher the

degree of daily disability.^[39] The clinical cutoff is 10 points. EuroQOL 5 dimensions 5-level (EQ-5D-5L) is the most commonly used scale worldwide for calculating quality-adjusted life years, which we will use for the assessment of economic evolution of medical technology. The EQ-5D-5L consists of 5 items that are scored from 0 (death) to 1 (in good health).^[40,41] Depressive symptoms were assessed with the Patient Health Questionnaire-9 (PHQ-9), which consisted of 9 items that scored on a 4-point Likert-scale (0, “not at all”; 1, “on several days”; 2, “half or more of days”; 3, “almost daily”). The minimum score is 0 and the maximum score is 27 (0–4, 5–9, 10–14, 15–19, and 20–27 indicate no, mild, moderate, moderate to severe, and severe symptoms, respectively). The cutoff score for clinically significant depressive symptoms is 10.^[42,43] Anxiety was measured with the Generalized Anxiety Disorder scale (GAD-7), which consisted of 7 items that assess the severity of GAD in the previous 2 weeks on a 4-point Likert-scale (0, “not at all”; 1, 1 episode; 2, “on half or more days”; 3, “almost daily”). The minimum score is 0 and the maximum score is 21 (0–4, 5–9, 10–14, and 15–21 indicate no, mild, moderate, and severe symptoms, respectively). The cutoff score for clinically significant symptoms of anxiety is 10.^[44] The therapist asked the patients about adverse event experiences in each session.

2.11. Sample size

In accordance with a previous study, we assumed that the expected change in the NRS was 1.9 and the standard deviation is 2.25.^[45] as a result, the required number of cases was 13 patients under the significance level of 5% on 1 side and the detection power of 80%. In this study, a total of 15 people was selected in consideration of dropouts and feasibility.

2.12. Statistical analyses

2.12.1. Data management. All data was properly managed by the submitting case report form to the Clinical Research Data Center. In this center, researchers entered all data using an access-log-restricted data system, which could be verified and created datasets. Independent data monitoring committees were regularly held and performed risk-based monitoring. After all intervention was finished, the responsible doctors confirmed their datasets and locked the data. Then the locked data were transferred to the Pharmaceutical Statistics Office of the Department of Clinical Trials, Chiba University Hospital.

2.12.2. Data analysis. The analysis cohort was 16 patients compared pre- to post-intervention. Baseline variables were compared using the Fisher exact test for categorical variables and the unpaired *t* test for continuous variables. For the primary analysis assessing treatment effects, the mean of change NRS and PCS from baseline to week 16 and their 95% CIs were estimated and tested whether they equaled 0 by *t* test (Post-Pre-Treatment). The baseline was set to day 8 when CBT began as session 1 (week 1). The NRS and PCS changes from baseline to week 8 were also evaluated for the secondary outcome assessing treatment effects. Similarly, the mean of changes PDAS, PHQ-9, GAD-7, and EQ-5D-5L from baseline to week 8 and 16, and their 95% CIs were estimated and tested whether they equaled 0 by *t* test. Cohen’s *D* of the changes for each variable and each week were also shown.

All *P*-values were 2 sided and the significance level was set to .05. Adjusting *P*-value for multiple comparisons was not considered in this study in order to ensure the power of each

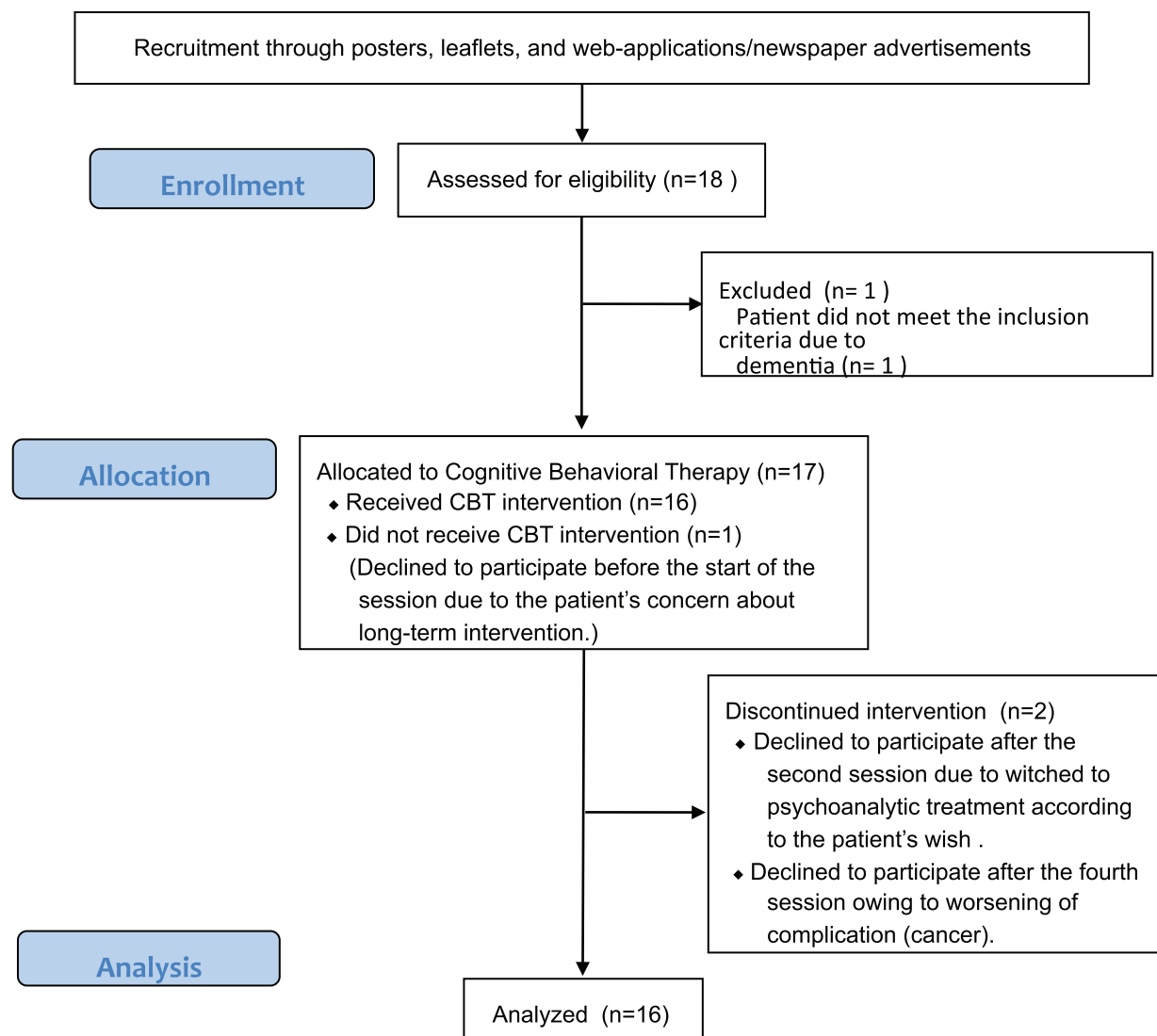


Figure 1. Flow chart of patient selection. This here show that flow diagram of the progress through the phases from enrollment to finally analysis. “n” in bracket each phase show the number of patients at that time. CBT=cognitive behavioral therapy.

test. All statistical analyses were performed by using SAS 9.4 (SAS Institute, Cary, NC).

3. Results

Figure 1 shows the patient recruitment flow diagram based on the Consolidated Standards of Reporting Trials guidelines.^[46] Eighteen patients were assessed for eligibility and 1 patient was excluded due to being diagnosed with dementia. Although 17 patients were enrolled in our CBT intervention program, 1 patient declined to participate prior to the beginning of the intervention. Finally, 16 patients underwent the CBT program. After the start of the CBT intervention, 2 more patients discontinued participation. One patient discontinued after the second session due to changed psychoanalytic treatment, according to the person's preference. The other patient discontinued after the fourth session due to worsening of their complication (cancer). Following the intention-to-treat, 16 patients were analyzed.

3.1. Patients' baseline information and clinical characteristics

Tables 2 and 3 present the baseline information of 16 patients (age = 30–77 years), and the onset age of pain symptoms ranged from 14 years to 74 years. Most (n = 14) of the patients did not work. Most of the patients (n = 14) had multiple painful areas. Most of the patients (n = 14) had physical comorbidity. Four patients had comorbid mental problems (Table 3).

3.2. Primary outcomes

The changes in NRS and PCS scores from pre-treatment to post treatment are shown in Table 4. The pain intensity measured by the NRS at week 16 from baseline showed no significant changes ($P = .657$). On the other hand, catastrophic cognition measured by the PCS at week 16 from baseline had significantly improved ($P = .001$), revealing a large effect size (Cohen's $d = 1.22$) based on the definition by Cohen.^[47] While the mean PCS at pre-intervention (n = 16, mean 31.44, SD 6.76) was over the clinical

Table 2
Baseline information of patients.

Patient (n = 16)	
Age (SD)	55.9 (15.4)
Sex(male), n (%)	6 (38)
Education history (SD)	14.4 (1.8)
Currently employed (%)	2 (13)
Chronic pain site (%)	6 (38)
low back	
upper back	1 (6)
neck	2 (13)
arms	1 (6)
legs	7 (44)
head	2 (13)
other	6 (38)
Duration of disease (SD)	13.41 (15.79)
Medication treatment (%)	12 (75)
Physical comorbidity (%)	7 (44)
Mental comorbidity (%)	4 (25)

For chronic pain site, duplicate answers were possible.
 SD = standard deviation.

cutoff point), the PCS at post-intervention reduced to normal ranges (n = 14, mean 21.71, SD 9.19).

3.3. Secondary outcomes

The changes in NRS and PCS scores from pre-treatment to middle-treatment are shown in Table 4. The pain intensity measured by NRS at week 8 from baseline showed no significant changes ($P = .799$). On the other hand, catastrophic cognition measured by PCS at week 8 from baseline was significantly improved ($P = .032$), revealing a moderate effect size (Cohen's $d = 0.57$),

The degree of disability in daily life measured by PDAS at week 16 from baseline showed significant reduction ($P = .012$, Cohen's $d = 0.42$). Depression measured by the PHQ-9 ($P = .001$, Cohen's $d = 0.69$) and anxiety measured by GAD-7 ($P = .008$, Cohen's $d = 0.47$) at week 16 from baseline also showed significant improvements, respectively. The mean scores on both PHQ-9 and GAD-7 at week 16 were found to be below the clinical threshold. There was no significant increase ($P = .223$, Cohen's $d = 0.34$) in the quality of life measured by the EQ-5D-5L at week 16. In the mid-evaluation, the scores on the PDAS, PHQ-9, GAD-7, and EQ-5D-5L at week 8 showed no significant changes, respectively.

3.4. Adverse events

Two patients reported non serious adverse events. One patient reported rib fracture by fall inside the house, and they recovered in 3 weeks. The other patient reported subcutaneous abscess due to worsening systematic lupus erythematosus, and recovered in a month by puncture drainage and pharmacotherapy. These adverse events, however, are considered to be unrelated to our CBT intervention. There were no serious adverse events reported during the study.

4. Discussion

Although pain intensity showed no significant change in the current study, there were significant improvements in catastroph-

ic cognition. Disability of daily life, depression, and anxiety also showed significant improvements.

Williams, Eccleston, and Morley^[7] in the Cochran database systematic review showed that CBT for chronic pain could improve pain intensity, daily activity, mood, and catastrophic cognition, compared to the usual treatment or waiting list controls with small to moderate effect sizes. In our study as well, although there was no reduction in pain intensity, the integrated CBT program enabled considerable improvement in catastrophic cognition, daily activity, and mood, despite the clinical setting.

Regarding outcomes, Åkerblom et al^[48] suggested that pain acceptance might play a pivotal role in CBT, even when it not explicitly targeted during treatment. In addition, they reported that pain acceptance was not related to pain intensity, which is in line with existing empirical findings and the treatment objectives. Although we set pain intensity measured by NRS as one of the primary outcomes, therapists discussed pain acceptance with patients in Session 2 about psychoeducation. This means that both the therapist and patient did not focus on reducing pain intensity. Instead, throughout the 16 sessions of CBT, the therapists tried to enable the patients to accept their pain and return to their daily lives. Patients acquired pain management skills through CBT to increase their activity levels. Further, they gained a sense of accomplishment. We think that, as a result, they no longer obsessed over their pain. We expect that patients' pain intensity will decrease over the next few years because they will have accepted their pain. Unfortunately, we did not measure pain acceptance using questionnaires such as the Chronic Pain Acceptance Questionnaire. In future studies, pain acceptance should be measured as one of the outcomes.

Regarding the components of CBT, we could compare the changes in outcomes between the first half of the program (Sessions 1 to 8) and the second half of the program (Sessions 9 to 16), since we evaluated the outcomes at 3 time points (pre-, mid-, and post-intervention) in the current study. Our results suggest that the first half of the program, including psychoeducation, attention shift, and cognitive restructuring, improves only catastrophic thinking, and the second half, including memory work, mental practice, video feedback, and behavioral experiments, improves catastrophic thinking, disability, and mood. However, it is still not known which session of the integrated CBT is most effective for which outcome. Single-case experimental designs using repeated measures and sequential introduction of an intervention might be useful to investigate this.^[50]

Regarding the number of CBT sessions, it is unclear whether 16 sessions are optimal. For example, what might happen if patients receive 20 CBT sessions by adding 4 behavioral experiment sessions or graded exposure sessions against fear of movement.^[51] Future studies could examine whether the outcomes show improvement.

Regarding the types of patients, patients were recruited from a real clinical setting. Thus, the sample consisted of patients aged over 65 years, including a 77-year-old patient, patients with cancer, fibromyalgia, cerebral palsy, and SLE. According to the latest version of the World Health Organization International Disease Classification Version 11 published in 2018, chronic pain is categorized to 7 groups as follows:

- (1) chronic primary pain,
- (2) chronic cancer pain,
- (3) chronic posttraumatic and postsurgical pain,
- (4) chronic neuropathic pain,

(5) chrc
(6) chrc
(7) chrc

Table 3
Patient characteristics and change in primary outcomes.

Patient	Age (yr)	Sex	Duration of disease (yr)	Pain locations	Completion	Physical comorbidity	Psychiatric comorbidity	Pharmacotherapy	NRS-pre	NRS-mid	NRS-post	PCS-pre	PCS-mid	PCS-pos
1	41	F	0.8	Both legs	Discontinued after the second session.	Gynecological cancer after chemotherapy	None	Pregabalin, duloxetine	5.4			30		
2	52	M	1.5	Low back, left leg, left hand	Discontinued after the fourth session.	Lumbar disc herniation, lumbar spondylolisthesis, bacterial infection bitten by cat.	None	Pregabalin, escitalopram, trazodone	8.2			30		
3	73	F	35.0	Right femur, both legs	Yes	Temporomandibular disorders, fractured wrist due to fall	None	Clonazepam, mirtazapine	6.7	6.0	7.8	22	28	24
4	37	M	3.0	Neck, low back	Yes	cerebral palsy	None	Pregabalin, acetaminophen	5.3	4.1	4.3	43	34	31
5	56	M	1.8	Both legs	Yes	None	None	Duloxetine, methotrexate, acetaminophen, tramadol, prednisolone, clonazepam, mexiletine	6.0	8.0	7.0	29	14	6
6	30	F	16.0	Right intercostal, left abdomen	Yes	Endometriosis, chocolate cyst	Generalized anxiety disorder	Clonazepam, etizolam	4.0	4.7	5.4	31	35	37
7	50	F	3.5	Left leg	Yes	Osteoarthritis	None	Neurotrophin, diazepam, duloxetine, valproic acid, clonazepam	6.0	5.0	5.0	22	15	15
8	40	F	5.0	Left heel	Yes	Complex regional pain syndrome, migraine, systemic lupus erythematosus	Moderate risk of suicide, bulimia nervosa	Pregabalin, acetaminophen, tramadol, celecoxib, methotrexate, prednisolone, lomerizine hydrochloride.	5.0	8.5	9.4	47	45	19
9	66	F	30.0	Left shoulder, neck, right ankle, low back, head	Yes	Hyperlipidemia, insomnia	Depression, dysthymia, obsessive compulsive disorder, post-traumatic stress disorder	Pregabalin, gabapentin, quetiapine, eperisone	7.6	8.3	8.6	34	36	34
10	72	M	47.0	Low back, upper back, abdomen	Yes	Lumbar disc herniation, spinal canal stenosis, intradural extramedullary tumor surgery, malignant thymoma surgery	none	Acetaminophen, tramadol	8.0	8.9	8.1	40	27	17
11	76	F	16.0	Low back, left knee	Yes	Right knee meniscus injury, glaucoma	None	Pregabalin, acetaminophen	4.0	6.1	3.6	30	19	15
12	37	M	2.0	head	yes	none	None	None	7.1	7.1	7.2	23	19	22
13	57	F	20.0	Low back, both legs, lower abdomen	yes	gallbladder stone	Moderate risk of suicide	Methylphenidate, atomoxetine	9.0	5.0	6.0	42	45	34
14	59	M	7.0	Left arm, left shoulder, left buttocks, low back	Yes	Cervical spondylosis, intervertebral foramen stenosis	None	Pregabalin, esczopion, loflazepate, trazodone	2.6	1.8	1.7	25	18	15
15	69	F	5.0	Right heel, both legs, both hands	Yes	Rheumatism, diabetes, hyperlipidemia	None	Pregabalin, acetaminophen, tramadol	3.0	2.6	3.5	32	23	14
16	77	F	3.0	Both soles	Yes	Peripheral neuropathy	None	None	8.0	9.8	9.0	31	15	21

NRS = Numerical Rating Scale, PCS = Pain Catastrophizing Scale.

Table 4
Efficacy outcomes.

Variable	Pre (1 wk)		Middle (8 wk)		Post (16 wk)		Change from pre to middle			Change from Pre to Post						
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	95%CI	P-value	Cohen's d	N	Mean (SD)	95%CI	P-value	Cohen's d
NRS	16	6.11 (1.94)	14	6.14 (2.42)	14	6.19 (2.35)	14	0.11 (1.65)	[-0.84, 1.06]	.799	0.01	14	0.16 (1.35)	[-0.62, 0.95]	.657	0.04
PCS	16	31.44 (6.76)	14	26.64 (10.82)	14	21.71 (9.19)	14	-5.00 (7.83)	[-9.52, -0.48]	.032	0.54	14	-9.93 (9.3)	[-15.30, -4.56]	.001	1.22
PDAS	16	23.56 (13.48)	14	24.00 (12.08)	14	18.50 (10.38)	14	-1.43 (5.09)	[-4.37, 1.51]	.313	0.03	14	-6.93 (8.88)	[-12.06, -1.80]	.012	0.42
PHQ-9	16	10.00 (5.98)	14	9.43 (6.31)	14	6.29 (4.58)	14	-1.43 (3.32)	[-3.35, 0.49]	.132	0.09	14	-4.57 (4.11)	[-6.94, -2.20]	.001	0.69
GAD-7	16	6.50 (4.66)	14	7.64 (5.73)	14	4.50 (3.67)	14	0.36 (3.93)	[-1.91, 2.63]	.739	0.22	14	-2.79 (3.36)	[-4.72, -0.85]	.008	0.47
EQ-5D-5L	16	0.51 (0.21)	14	0.51 (0.17)	14	0.57 (0.12)	14	0.01 (0.16)	[-0.08, 0.11]	.785	0	14	0.07 (0.21)	[-0.05, 0.19]	.223	0.34

EQ-5D-5L = EuroQOL 5 dimensions 5-level, GAD-7 = generalized anxiety disorder scale, NRS = numerical rating scale, PCS = pain catastrophizing scale, PDAS = pain disability assessment scale, PHQ-9 = Patient health questionnaire-9, SD = standard deviation.

Ideally, the effectiveness of the integrated CBT program should be evaluated for each category.

Among the 16 patients with chronic pain who underwent our integrated CBT program, 2 patients discontinued due to their personal circumstances: 1 patient discontinued after completing the second session, and the other discontinued after the fourth CBT session. Fourteen patients completed the CBT program in 16 weeks. No adverse events were reported. The results suggest that our integrated CBT program can be used to treat patients suffering from chronic pain. It is a safe and feasible method of treatment.

In future studies, we think that it is necessary to design “stepped care” for chronic pain. In the UK, the National Institute for Health and Care Excellence clinical guideline recommends stepped care for depression. In stepped care, patients typically start with a low-intensity, low-cost treatment such as guided self-help CBT; patients who do not respond to low-intensity CBT move to a high-intensity treatment such as individual CBT. A systematic review and meta-analysis showed that stepped care had a moderate effect on depression (pooled 6-month between-group effect size (Cohen's d) was 0.34).^[49]

We believe that stepped care for chronic pain is also useful. While patients with mild chronic pain start with low intensity CBT, we propose that patients with severe chronic pain after poor response to low-intensity CBT can receive high-intensity CBT developed in the present study. Nonetheless, future studies on stepped care for chronic pain are needed. Moreover, it is necessary for multicenter studies with large samples to investigate which component of our CBT protocol is more effective than Otis' traditional protocol.^[11,12]

4.1. Strength and limitations

This integrated CBT program is feasible in terms of providing pain management skills to patients with chronic pain in a clinical setting.

However, this study has a few limitations. First, the sample size was too small to apply CBT on patients suffering from different types of chronic pain. Therefore, it is necessary to categorize patients with chronic pain and to design clinical studies with an adequate sample size to include different types of chronic pain. The second limitation is the self-evaluation method to assess pain intensity. Most patients had multiple painful body parts, and NRS scores were evaluated by mixing scores from multiple painful parts or changing scores to a new painful part. Even if the pain intensity in 1 body part improved, the patient evaluated other body parts as painful. When a patient has multiple pain areas, pain intensity should be evaluated in each body part in

future studies. The third limitation is our having used only acute-phase data after CBT. We should also collect follow-up data to verify persistent effectiveness.

The fourth limitation of this study is its design, that of a single-arm trial. It will be necessary to verify the efficacy of the program with a control group and 2-arm randomized controlled trials in the future.

5. Conclusion

This study suggests that our integrated CBT program can be provided to patients suffering from various types of chronic pain, in a real clinical setting. Furthermore, CBT may also improve the catastrophic cognition, disability in daily life, depression, and anxiety. Future large-scale controlled studies are needed to investigate the effectiveness of the program. Meanwhile, we have already designed and started a pilot randomized controlled trial, “The Effect of Internet-based CBT with Real-Time Therapist Support Via a Video Conference for Patients with Chronic Pain: a Study Protocol” (UMIN000031124) on telemedicine using a video conference system, and will also provide modified CBT strategies developed in this study.

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Author contributions

KT and ES contributed to the design of this study and development of the original protocol; KT was responsible for drafting most of the initial manuscript. KY prepared guidelines for the treatment delivery and contributed to the study design. RT were responsible for developing a statistical analysis plan and assisted in the preparation of the manuscript. NN, RT, TY, and KK developed new, important contents for this protocol and critically revised the article. All authors have approved the final version of the manuscript. All authors are accountable for any questions related to the accuracy or integrity of any part of this work.

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