J. Phys. Ther. Sci. 36: 750–755, 2024

The Journal of Physical Therapy Science

Case Study

Effect of long-term rehabilitation on takotsubo syndrome-induced severe intensive care unit-acquired weakness: a case report

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Abstract. [Purpose] To examine the effectiveness of acute and outpatient cardiac rehabilitation for severe intensive care unit (ICU)-acquired weakness. [Participant and Methods] A 79-year-old woman, diagnosed with takotsubo syndrome. A percutaneous catheter-based transvalvular left ventricular assist device was used from day 2 to day 8, extracorporeal membrane oxygenation from day 3 to day 9, and inotropic support from day 1 to day 15. The patient was weaned from the ventilator on day 59, transferred to another hospital on day 67, and discharged home on day 152. From days 16 to 65 and 177 to 262, she underwent inpatient rehabilitation and outpatient cardiac rehabilitation, respectively, at our hospital. [Results] After inpatient rehabilitation at our hospital, her Medical Research Council score improved from 16 to 46. In outpatient cardiac rehabilitation, her 6-minute walk distance improved from 385 to 473 m, and her Kansas City Cardiomyopathy Questionnaire score improved from 88.6 to 100. [Conclusion] The results suggest that acute rehabilitation can effectively improve muscle strength, whereas outpatient cardiac rehabilitation can effectively improve exercise tolerance and quality of life in patients with severe ICU-acquired weakness.

Key words: Outpatient cardiac rehabilitation, Acute rehabilitation, Physical therapy

(This article was submitted Jun. 29, 2024, and was accepted Aug. 4, 2024)

INTRODUCTION

Acute diffuse muscle weakness in critically ill patients is termed intensive care unit-acquired weakness (ICU-AW) in the absence of a plausible etiology other than the critical illness and its treatments[1)]. Muscle weakness is associated with an increased risk of mortality in these patients; the more severe the muscle weakness, the higher the risk of mortality[2)]. While the muscle weakness in survivors of patients suffered from ICU-AW usually resolves within 12 months[3)], it has been reported that reduced walking ability and poor quality of life (QOL) can persist for more than 5 years[4)]. The Medical Research Council (MRC)-sum score, which ranges from 0 to 60, has been used to obtain the diagnosis of ICU-AW[5)]. An ICU patient with an MRC-sum score <48 (mean score of each muscle evaluated <4) is considered to have ICU-AW[1)], and that with an MRC sum score <36 (mean score <3) is considered to have severe ICU-AW[6)]. To our best knowledge, there have not been any large studies on the functional outcomes of patients with severe ICU-AW. Moreover, there have been only a few case reports describing the long-term functional outcomes of patients with extremely severe muscle weakness (MRC sum score <24 [mean score <2])[7–9)].

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Outpatient cardiac rehabilitation (CR) may be effective for prolonged functional impairment and reduced QOL in patients with ICU-AW. Continuous CR, including outpatient CR, has been reported to prevent recurrence of cardiac disease and improve life prognosis, as well as improving exercise tolerance and QOL[10–12]. However, there are no reports that long-term rehabilitation, including outpatient cardiac rehabilitation, is effective for functional impairment and QOL in patients with extremely severe ICU-AW.

We treated a patient with takotsubo syndrome and extremely severe ICU-AW. The patient underwent acute rehabilitation therapy starting from her stay in the cardiac care unit (CCU). The patient could not be discharged to her home from our acute-care hospital, but was sent to a convalescent rehabilitation hospital and then discharged to her home. She then received outpatient CR, which resulted in greatly improved physical function. Herein we report this case.

CASE

Figure 1 shows the timeline of the patient's medical treatment and rehabilitation, starting from her admission to our hospital and finishing with the end of her outpatient CR.

The patient was a 79-year-old Japanese woman with a history of hypertension. She could perform her activities of daily living without help. She had been having marital problems for 3 months and had been feeling unwell for two days prior to admission. On the day of admission, she was transported to our hospital because of low blood pressure and difficulty in breathing. Upon arrival at the hospital, a 12-lead electrocardiogram showed ST-segment elevation in leads V1 to V6, and a chest x-ray showed ground-glass opacities in the left lung. Echocardiography showed systolic dysfunction at the apex; a left ventricular ejection fraction (LVEF) of 48.6%; and a left ventricular outflow tract velocity time integral of 7.8 cm, which is markedly lower than the cut-off value of 15.8 cm that is associated with a poor clinical outcome[13]. Coronary angiography was performed immediately and was negative for significant stenosis of the coronary arteries. She was diagnosed with Takotsubo syndrome that was caused by marital problems as a psychological stressor and pneumonia as a physical stressor, and was admitted to the CCU.

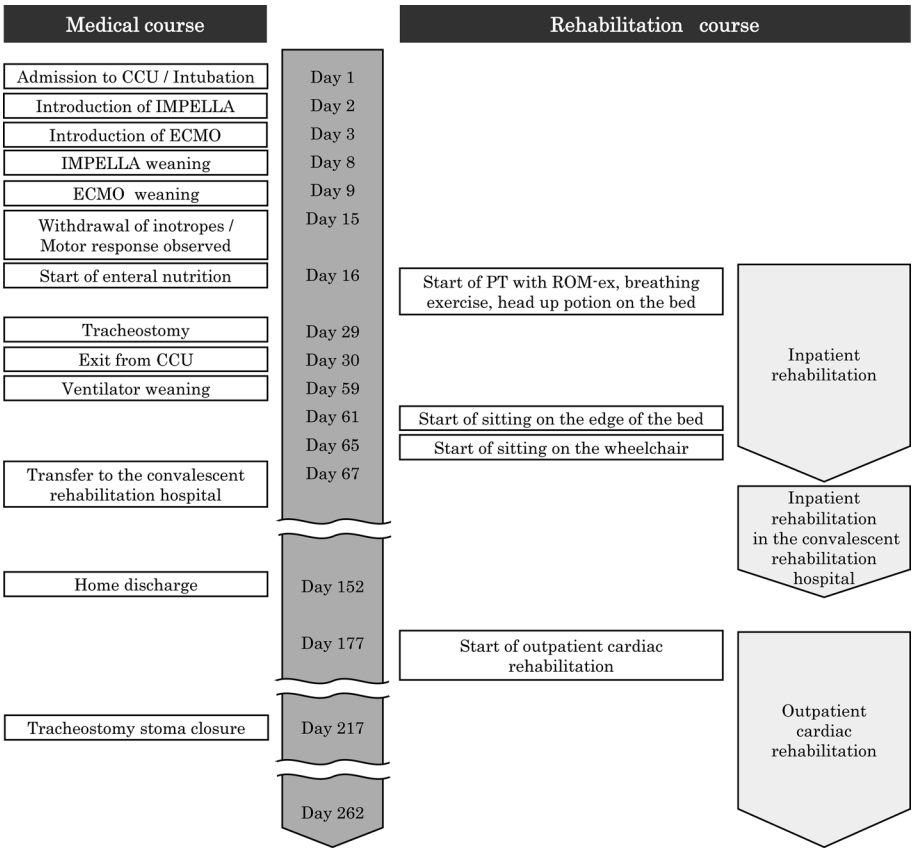

Fig. 1. Timeline of medical treatment and rehabilitation.
Days since onset shown in the center, progress with medical treatment shown on the left, and progress with rehabilitation shown on the right. CCU: cardiac care unit; IMPELLA: transvalvular left ventricular assist device; ECMO: extracorporeal membrane oxygenation; PT: physical therapy; ROM-ex: range of motion exercise.

Immediately after admission, the patient was placed on mechanical ventilation to treat her circulatory failure. She was supported by a percutaneous catheter-based transvalvular left ventricular assist device (Abiomed Japan Inc., Ltd., Tokyo, Japan; IMPELLA) for 7 days from the day after her admission to the CCU (days 2 to 8 of hospitalization) and extracorporeal membrane oxygenation (ECMO) for 7 days from days 3 to 9 of hospitalization. The patient was sedated with midazolam from days 1 to 11, and rocuronium from days 3 to 10. Inotropic agents were given from days 1 to 15, and hydrocortisone from days 3 to 11. The patient's worst sequential organ failure assessment score of 12 and her worst arterial lactate level of 9.8 mmol/L were obtained before the use of a ventricular assist device. Enteral nutrition was started and a spontaneous breathing trial (SBT) was performed on day 16. The SBT found that her tidal volume was 140 mL, her respiratory rate was 30 breaths/min, and the patient also complained of dyspnea. Therefore, she could not be weaned from the ventilator until day 59. The patient underwent tracheostomy on day 29, left the CCU on day 30, and was weaned from the ventilator on day 59.

Antibiotics were administered from days 1 to 49 to treat the patient's concomitant pneumonia. On day 67 of her hospitalization, she was transferred to a convalescent rehabilitation hospital.

At the request of the attending physician, physical therapy (PT) was started on day 16 of the patient's stay in the acute hospital. PT consisted of passive range of motion exercises (ROM-ex), active-assisted ROM-ex, breathing exercises, and postural changes such as a head-up position in bed. PT was performed 5 times/week, 20–40 minutes per session. On days 16 and 17, the patient's MRC-sum score was 16 (wrists and ankles: 2, others: 1), indication she was severe ICU-AW (MRC sum score <36). When the patient's muscle strength improved (Fig. 2), her PT program was gradually changed from passive and active-assisted ROM-ex to active ROM-ex, and an antigravity exercise was added.

At the beginning of PT, the patient often complained of pain when performing passive ROM-ex, but her complaints decreased with increased muscle strength. The patient was able to write sentences on day 57, began sitting on the edge of the bed on day 61, and sat in the wheelchair and stood with assistance on day 65. Until transfer to the convalescent rehabilitation hospital (day 67), the patient's MRC-sum score improved from 16 (wrists and ankles: 2, other: 1) to 46 (hips: 2, other: 4) in 50 days, but did not exceed the ICU-AW cut-off value of 48 (Fig. 2). The Barthel Index remained 0 until transfer (Table 1).

The patient was transferred to the convalescent rehabilitation hospital from our acute-care hospital on day 67 and continued inpatient rehabilitation. She was discharged home from the convalescent rehabilitation hospital at a total of 151 days after her admission to the CCU of our hospital. Subsequently, the patient visited our hospital as an outpatient. Outpatient echocardiography was negative for left ventricular asymmetry, and showed a LVEF of 67.2% and moderate mitral regurgitation. The patient's blood level of brain natriuretic peptide was 386.7 pg/mL. After consultation with her physician and rehabilitation staff, her physician prescribed CR for chronic heart failure, and outpatient CR was started on day 177 after her initial hospitalization. After 86 days of inpatient rehabilitation at the convalescent hospital, the patient's Barthel Index had improved to 100 and her MRC-sum score to 53. Thus, the patient no longer met the diagnostic criteria of ICU-AW. However, her muscle weakness and exercise intolerance remained, with a 6-minute walk distance (6MWD) of 385 m (Table 1).

Outpatient CR was performed twice weekly for 3 months at 60 minutes per session. With the patient monitored by electrocardiography and blood pressure assessments, each session consisted of a warm-up, lower limb resistance training, and 30 minutes of aerobic exercise on a cycle ergometer. As cardiopulmonary exercise testing could not be performed because of the patient's tracheostomy stoma, anaerobic metabolic thresholds could not be measured. In addition, the patient's heart rate could not be used as a measure of exercise intensity because she was taking a beta-blocker. Therefore, the patient's exercise intensity was adjusted to 12–13 on the Borg Rating of Perceived Exertion Scale. The patient pedaled on a cycle ergometer with a power output of 15–25 watts, which is equivalent to 2.9–3.6 metabolic equivalents (METs). The patient's exercise tolerance was assessed according to the 6MWD test. The patient was instructed by the physical therapists and nurses to self-monitor her blood pressure, pulse rate, body weight, and the presence or absence of signs of heart failure daily, which she was able to do. Although she was also instructed to perform exercises such as brisk walking for 30 minutes 1–3 times weekly, she did not exercise as much as instructed. The patient also received nutritional advice from a dietician. The patient had a generally balanced diet, but ate noodles for lunch, and had a daily energy intake of 1,600 kcal and a salt intake of 8 g,

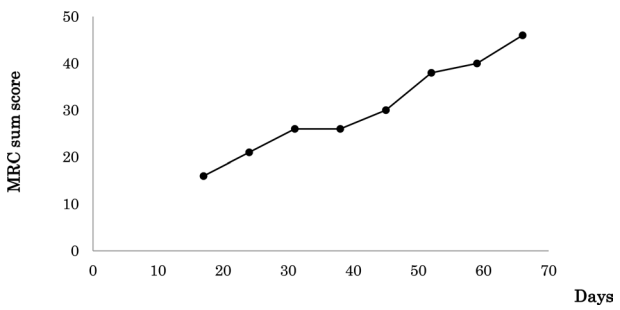

Fig. 2. Progress of MRC sum score from the start of rehabilitation to transfer to another hospital.
MRC: Medical Research Council.

Table 1. Changes in body composition, physical function, functional independence and quality of life

	Day 16	Day 67	Day 177	Day 262
Body weight (kg)	51.5	47.3	49.3	50.1
Body mass index (kg/m^2)	20.1	18.5	19.3	19.6
Extracellular water ratio			0.411	0.399
Skeletal muscle index (kg/m^2)			6.1	5.9
MRC sum score	16	46	53	58
Grip strength (kgf)		13.2 / - *	10.4 / 8.0	14.1 / 12.0
Knee extension strength (kgf)			15.9 / 15.4	22.5 / 20.5
Knee extension strength/body weight (%)			32.3 / 31.2	44.9 / 40.9
Gait speed (m/sec)			1.01	1.07
SPPB			10	12
6-minute walk distance (m)			385	473
Barthel Index	0	0	100	100
KCCQ			88.6	100

*Not measurable as less than 5 kgf. MRC: Medical Research Council; SPPB: Short Physical Performance Battery; KCCQ: Kansas City Cardiomyopathy Questionnaire.

which was slightly higher than the target salt intake. The dietitian instructed her on the need for dietary therapy for patients with cardiac disease and how to eat a balanced diet and reduce salt intake. The patient underwent tracheostomy closure on day 217, after which outpatient CR was suspended for 2 weeks.

After outpatient CR for 3 months, the patient's MRC sum score improved from 53 to 58, knee extension strength/body weight improved from 0.323/0.312 kgf/kg to 0.449/0.409 kgf/kg, Short Physical Performance Battery improved from 10 to 12, and 6MWD improved from 385 m to 473 m. In addition, the Kansas City Cardiomyopathy Questionnaire (KCCQ) score, a measure of symptoms, physical and social limitations and quality of life (QOL) related to heart failure, improved from 88.6 to 100.

Written informed consent was obtained from the participant included in the study.

DISCUSSION

This case is valuable because it shows that both acute inpatient rehabilitation and outpatient CR may be effective in patient with extremely severe ICU-AW, which is considered to be a long-term residual, in the same case. In our patient, muscle weakness associated with severe ICU-AW after intensive care was improved by acute rehabilitation in our hospital, but her ability to perform activities of daily living (ADL) did not improve during her hospital stay. Following inpatient rehabilitation at the convalescent hospital, her ability to perform ADL improved and she was discharged home. Her exercise tolerance and QOL further improved at home during 3 months of outpatient CR.

Although it has been reported that muscle weakness in survivors of ICU-AW usually recovers within 12 months[3], there are no large studies on the functional outcome of patients with extremely severe ICU-AW (such as an MRC-sum score <24 [mean score of each muscle evaluated <2). However, several case reports have demonstrated that rehabilitation for patients with extremely severe ICU-AW can lead to their functional improvement[7–9]. The MRC-sum score of our patient was improved from 16 to 46 by rehabilitation during her 50-day stay at our acute-care hospital. At the start of her rehabilitation program on day 16, our patient was unable to move her limbs independently and complained of pain during passive ROM-ex, which suggested the impending onset of joint contractures. We think that rehabilitation exercises such as passive ROM-ex prevented the development of joint contractures due to her immobility, and may have contributed to her improved muscle strength. In addition, active and active-assisted ROM-ex may have prevented secondary muscle weakness due to immobility, and also contributed to her improved muscle strength. It was suggested that acute rehabilitation initiated when a patient is in the ICU or CCU has a beneficial effect on recovery from extremely severe muscle weakness due to severe ICU-AW. On the other hand, if she had started rehabilitation sooner than day 16, her muscle strength might have been additionally increased. It was considered desirable to start physical therapy earlier and there is a need to improve collaboration between the attending physician and the rehabilitation team.

Outpatient CR performed for several months after discharge from an acute-care hospital has led to reduced risks of the recurrence of cardiovascular events and mortality, as well as improved exercise tolerance and QOL[10–12]. The exercise tolerance and QOL of our patient were markedly improved by outpatient CR performed for 3 months after her discharge from the rehabilitation facility. The patient's 6MWD improved from 385 m to 473 m, which is greater than the minimal clinically important difference of 0.14.0 to 30.5 m[14]. Grundtvig et al. reported that a cut-off value of 380 m was a poor prognostic indicator in patients with heart failure[15]. After 3 months of outpatient CR, our patient markedly exceeded the cut-off value. The

patient's KCCQ score improved from 88.6 to 100, a perfect score, indicating that her subjective symptoms and limitations associated with heart failure had disappeared. While it has been reported that reduced walking ability and poor QOL persist 5 years after intensive care[4], our patient made an excellent recovery after outpatient CR. Additionally, a study reported that comprehensive disease management programs for heart failure patients reduce mortality and the frequency of hospitalization, and may improve QOL[16]. Comprehensive multidisciplinary interventions for our patient by physicians, nurses, physical therapists, and dieticians may have prevented exacerbations of heart failure and contributed to her improved QOL. Another possible reason for her recovery is Takotsubo syndrome. In-hospital mortality in patients with Takotsubo syndrome who present with cardiogenic shock has been reported to be as high as 10%, while cardiac function in survivors has been reported to return to normal[17, 18]. Indeed, in our patient, her abnormal ventricular wall motion had resolved, although there was moderate mitral regurgitation at the start of outpatient CR. The recovery of cardiac function may have contributed to the improvement in QOL and exercise tolerance.

This case suggests that long-term rehabilitation through acute hospital, convalescent hospital and outpatient CR can be effective in patients with severe ICU-AW. However, some critically ill patients may not be offered the opportunity to receive outpatient CR after discharge. It has been reported that decline in ADL can persist for several months after intensive care[19], and it is not uncommon for older patients not to be linked to outpatient CR provided in acute hospitals because they cannot return home directly from the acute hospital. This case was also unable to be discharged home directly from an acute hospital due to a decline in ADL, but was discharged home after rehabilitation in the convalescent hospital. Fortunately, the patient then had the opportunity to attend our hospital and, following discussions between the attending physician and the rehabilitation team, an outpatient CR was offered. In order to provide long-term and effective rehabilitation, it is considered important for medical institutions to work together, for attending physicians and rehabilitation teams to work together, for patients to be informed about outpatient CR and for activities to promote outpatient CR.

In conclusion, the results suggested that acute rehabilitation can be effective in improving muscle strength in patients with severe ICU-AW and that outpatient CR can be effective in improving their exercise tolerance and quality of life. It was also suggested that outpatient CR is important even in patients with severe cardiac disease who are discharged home after rehabilitation in a convalescent hospital.

Conflict of interest

The authors declare that there are no conflicts of interest.

REFERENCES

1) Stevens RD, Marshall SA, Cornblath DR, et al.: A framework for diagnosing and classifying intensive care unit-acquired weakness. Crit Care Med, 2009, 37: S299–S308. [Medline] [CrossRef]
2) Hermans G, Van Mechelen H, Clerckx B, et al.: Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched analysis. Am J Respir Crit Care Med, 2014, 190: 410–420. [Medline] [CrossRef]
3) Fan E, Dowdy DW, Colantuoni E, et al.: Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. Crit Care Med, 2014, 42: 849–859. [Medline] [CrossRef]
4) Herridge MS, Tansey CM, Matté A, et al. Canadian Critical Care Trials Group: Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med, 2011, 364: 1293–1304. [Medline] [CrossRef]
5) De Jonghe B, Sharshar T, Lefaucheur JP, et al. Groupe de Réflexion et d'Etude des Neuromyopathies en Réanimation: Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA, 2002, 288: 2859–2867. [Medline] [CrossRef]
6) Hermans G, Clerckx B, Vanhullebusch T, et al.: Interobserver agreement of Medical Research Council sum-score and handgrip strength in the intensive care unit. Muscle Nerve, 2012, 45: 18–25. [Medline] [CrossRef]
7) Trees DW, Smith JM, Hockert S: Innovative mobility strategies for the patient with intensive care unit-acquired weakness: a case report. Phys Ther, 2013, 93: 237–247. [Medline] [CrossRef]
8) Chillura A, Bramanti A, Tartamella F, et al.: Advances in the rehabilitation of intensive care unit acquired weakness: a case report on the promising use of robotics and virtual reality coupled to physiotherapy. Medicine (Baltimore), 2020, 99: e20939. [Medline] [CrossRef]
9) Morimoto Y, Sekino M, Eishi K, et al.: Recovery of muscle weakness and physical function in a patient with severe ICU-acquired weakness following pulmonary embolism: a case report. Clin Case Rep, 2018, 6: 1214–1218. [Medline] [CrossRef]
10) Dibben G, Faulkner J, Oldridge N, et al.: Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev, 2021, 11: CD001800. [Medline]
11) Long L, Mordi IR, Bridges C, et al.: Exercise-based cardiac rehabilitation for adults with heart failure. Cochrane Database Syst Rev, 2019, 1: CD003331. [Medline]
12) Pandey A, Parashar A, Kumbhani D, et al.: Exercise training in patients with heart failure and preserved ejection fraction: meta-analysis of randomized control trials. Circ Heart Fail, 2015, 8: 33–40. [Medline] [CrossRef]
13) Omote K, Nagai T, Iwano H, et al.: Left ventricular outflow tract velocity time integral in hospitalized heart failure with preserved ejection fraction. ESC Heart Fail, 2020, 7: 167–175. [Medline]
14) Bohannon RW, Crouch R: Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. J Eval Clin Pract, 2017, 23: 377–381. [Medline] [CrossRef]

15) Grundtvig M, Eriksen-Volnes T, Ørn S, et al.: 6 min walk test is a strong independent predictor of death in outpatients with heart failure. ESC Heart Fail, 2020, 7: 2904–2911. [Medline] [CrossRef]
16) Roccaforte R, Demers C, Baldassarre F, et al.: Effectiveness of comprehensive disease management programmes in improving clinical outcomes in heart failure patients. A meta-analysis. Eur J Heart Fail, 2005, 7: 1133–1144. [Medline] [CrossRef]
17) Di Vece D, Citro R, Cammann VL, et al.: Outcomes associated with cardiogenic shock in Takotsubo Syndrome. Circulation, 2019, 139: 413–415. [Medline] [CrossRef]
18) Sharkey SW, Windenburg DC, Lesser JR, et al.: Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol, 2010, 55: 333–341. [Medline] [CrossRef]
19) Sidiras G, Patsaki I, Karatzanos E, et al.: Long term follow-up of quality of life and functional ability in patients with ICU acquired weakness—a post hoc analysis. J Crit Care, 2019, 53: 223–230. [Medline] [CrossRef]