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Original Article

Effects of continuous mobility training versus hand bicycle exercise in individuals with prolonged mechanical ventilation: A randomized-controlled trial

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ABSTRACT

Objectives: This study aims to examine the clinical effects of the continuous mobility training in participants with prolonged mechanical ventilation.

Patients and methods: Between February 2023 and June 2023, this randomized-controlled study included a total of 56 participants (33 males, 23 females; mean age: 70.1±15.9 years; range, 35 to 91 years) who were randomly assigned with 28 participants in the experimental group and 28 participants in the control group. The experimental group underwent routine ventilator weaning plan and continuous mobility training plan. The control group underwent the routine ventilator weaning plan and hand bicycle training. The length of mechanical ventilation, length of stay at the respiratory care center, total length of hospital stay and success rate of ventilator weaning were analyzed.

Results: The mean length of mechanical ventilation (17.1±10.5 *vs.* 29.0±13.4 days, p=0.000) and stay at the respiratory care center (21.5±9.6 *vs.* 34.8±14.6 days, p=0.000) were shorter in the experimental group than the control group, indicating statistically significant differences. The mean total length of hospital stay of the experimental was shorter than the control groups (59.3±21.5 *vs.* 70.5±24.4 days), indicating a statistically significant difference (p=0.075). The success rate of ventilator weaning in the experimental group and control group were 89.3% and 67.9%, respectively, without statistically significant difference (p=0.051).

Conclusion: The continuous mobility training in individuals with prolonged mechanical ventilation can reduce the length of mechanical ventilation and stay at the respiratory care center, but has no significant benefit for the total length of hospital stay and the success rate of ventilator weaning.

Keywords: Exercise, mechanical ventilation, ventilator weaning.

Advances in care technology related to the intensive care unit (ICU) and mechanical ventilation have improved the short-term survival of more individuals who are dependent on mechanical ventilation.[1] In the first 18 to 69 h of using a mechanical ventilation, the strength of the diaphragm and limb muscles of the individuals decreases rapidly due to bed rest, sedatives, muscle relaxants and the pathology of the patient.[2] Muscle atrophy also accompanies the decrease in muscle mass, muscle strength and aerobic benefit, which leads to a decline in physical activity function and poor treatment prognosis.[3] Difficulty in weaning from the ventilator affects the patient's future quality of life and increases the expenses related to health care and mortality.[4] Individuals undergoing prolonged mechanical ventilation gradually suffer from muscle atrophy due to their prolonged bed rest and reduced activities.[5] The incidence of prolonged mechanical ventilation accounted for approximately 5 to 13% of all individuals who used mechanical ventilation.[6] The number of individuals with

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prolonged mechanical ventilation has growing over the years, and the overall resource consumption has greatly increased.[7]

The primary factors which cause prolonged mechanical ventilation are severity of diseases, sepsis and shock before admission to the ICU,[8] and are related to mechanical ventilation.[9] This would cause the delay in discontinuing mechanical ventilation,[10] prolong the length of hospital stay, prolong the length of mechanical ventilation, and increase the failure rate of discontinuing mechanical ventilation and patient mortality.[11]

The exercise can reduce inflammation, and promote muscle strength and daily living function. Early exercise enabled individuals with mechanical ventilation to improve their physical activity function, shorten the length of mechanical ventilation and hospitalization,[12] and improve the physical function at discharge.[13] Some researches have shown that there is a significant difference in the length of mechanical ventilation, physical function and quality of life.[14] Early mobilization is one of the clinical challenges in individuals who use mechanical ventilation.[15] The early mobilization protocol of participants using a mechanical ventilation has its diversity, which warrants further investigation.[16-18]

In the literature, there are some researches regarding early mobility program for the participants with prolonged mechanical ventilation. The contents of early mobility program focused on the mobility levels. However, there is no research about the duration of mobility training. In the present study, we hypothesized that whether individuals with prolonged mechanical ventilation underwent continuous mobility training, the duration of training session could increase the success rate of mechanical ventilation weaning (weaning for more than five days), reduce the length of mechanical ventilation, reduce the length of stay in the respiratory care center, and reduce the total length of hospital stay. We, therefore, aimed to examine the clinical effects of the continuous mobility training in participants with prolonged mechanical ventilation.

PATIENTS AND METHODS

This single-center, prospective, concealed allocation, evaluator-blind, intention-to-treat, randomized-controlled study was conducted at Taichung Tzu Chi Hospital, Department of Respiratory Care Center between February 2023 and June 2023. Individuals over 18 years of age, who used mechanical ventilation, were transferred from the ICU to the respiratory care center for mechanical ventilation weaning, and were evaluated by a physician enrolled in the study. If eligible, the physician would conduct further examinations to ensure the suitability and safety of the participants, and the reasons for ineligibility for inclusion would be noted in the log. Inclusion criteria were as follows: age over 18 years; using mechanical ventilation for at least 6 h per day in the ICU, having previously failed to wean and transferred to the respiratory care center for weaning; stable vital signs, i.e., respiratory rate between 12 and 40 bpm, absence of cardiac arrhythmias, heart rate between 50 and 130 bpm, mean arterial pressure between 60 and 120 mmHg, oxygen saturation >92%; and ability to understand simple instructions and agree to participate in this research program after explanation. Exclusion criteria were as follows: unconsciousness, severe cognitive impairment, or inability to follow instructions; severe heart failure (New York Heart Association [NYHA] Class ≥3); diagnosis of terminal illness and undergoing palliative care; and Assessment by other attending physician that the participant's condition, progression of disease course or treatment plan were not suitable for exercise therapy. A total of 83 participants were transferred from the ICU to the respiratory care center for mechanical ventilation weaning. Of them, 27 were excluded, among which 22 did not meet the enrollment criteria and five refused to participate in this study. Finally, a total of 56 participants (33 males, 23 females; mean age: 70.1±15.9 years; range, 35 to 91 years) were randomly assigned with 28 participants in the experimental group and 28 participants in the control group (Figure 1). Written informed consent was obtained from each participant. The study protocol was approved by the Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation Research Ethics Committee (Date: 14.10.2019, No: REC108-28). The study was conducted in accordance with the principles of the Declaration of Helsinki. The study is registered at ClinicalTrial.gov with the number of NCT05688267.

The participants were randomly divided into the experimental and control group in a one-to-one ratio. The research assistant placed the number plate in an opaque and sealed envelope to ensure concealed

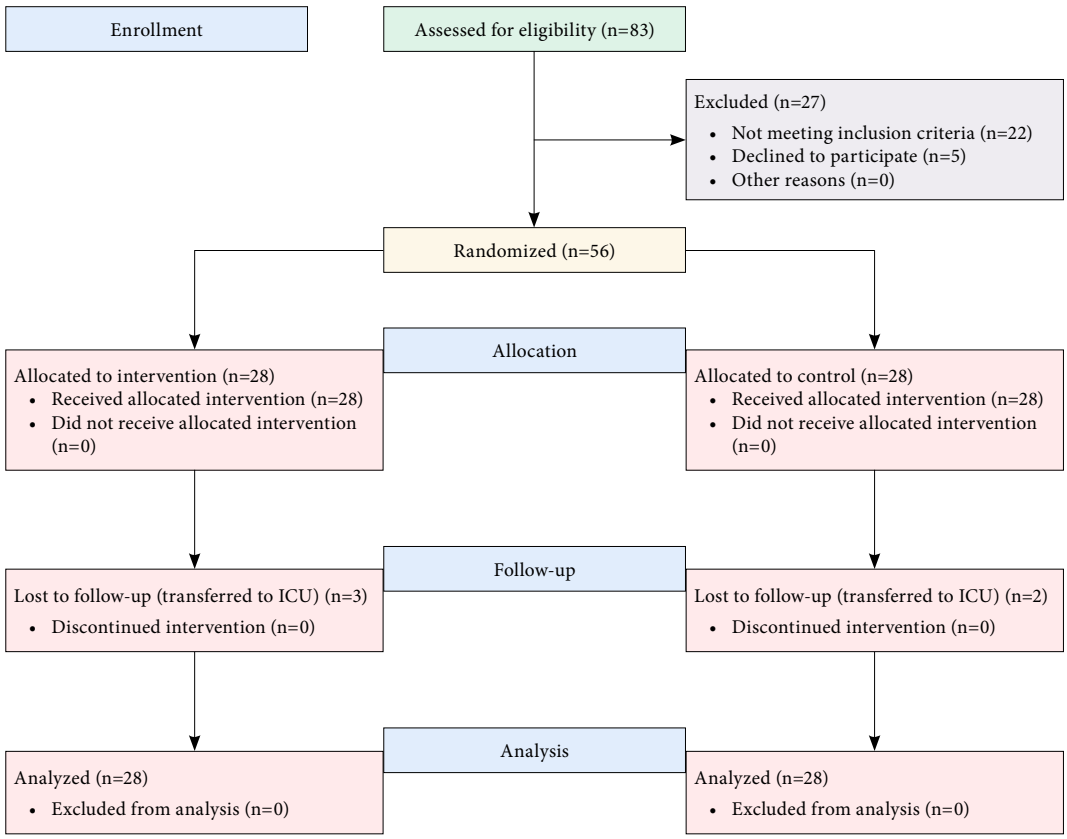

Figure 1. Study flowchart.

allocation. The order of allocation was randomized by the computer. The control group underwent the routine mechanical ventilation weaning plan and hand bicycle training, while the experimental group underwent the routine mechanical ventilation weaning plan and continuous mobility training. Owing to the nature of the exercise intervention, it is impossible to maintain blinding of the team members and participants. However, the physical therapists who evaluated the main outcome were separated from those who performed the therapy; thus, the evaluators were blinded. The content of the continuous mobility training program depended on the evaluation results and the physical responses of the participants. The treatment frequency of continuous mobility training was five times a week, once a day from Monday to Friday.

Intervention protocol

Control group: Participants of control group formed the routine care group, received the routine mechanical ventilation weaning plan and underwent hand bicycle training. The physicians assessed the participants and appropriately adjusted the settings of the mechanical ventilation modules to gradually reduce the participants' dependence on mechanical ventilation. Hand bicycle training was conducted by nurse practitioners once a day. The participants' bedheads were raised, and the participants held the cycle ergometer with both hands once they could tolerate upright position for 20 min. The training intensity was targeted at the level of symptom limitation, on the basis of the modified Borg CR10 RPE scale of 3-5. Intermittent and short-term periods of rest were allowed for participants to achieve the goal of a total of 20 min exercise session.

Experimental group: Participants of the experimental group were given continuous mobility training in addition to the routine mechanical ventilation weaning plan. The protocol was divided into five levels and focused on duration - a modification from Dong et al.[19] The physicians were responsible for evaluating whether the participants had any contraindication before and during enrollment. If any contraindication occurred at any time point, such as hypoxemia or unstable vital sign, the treatment would be

terminated immediately. The continuous mobility training would be performed once a day from Monday to Friday. During the whole continuous mobility training process, the exercise progress would be increased gradually, depending on the tolerance and stability of the participants. The goal setting of each training exercise session was that the participants could undergo the training duration for 20 min continuously.

The continuous mobility training adopted grading exercise level, which was evaluated and implemented by physical therapists, and focused on continuous mobility training courses with different levels. At each stage, the participants were instructed to perform spontaneous breathing exercise, which were confirmed by the physical therapists. In the first stage, the participants' bedheads were raised, and the trunk were kept upright on the bed. In sitting posture training, chest expansion training and deep breathing training was performed. The training goal was that the participants should be able to sit in bed for at least 20 min, and after training, the modified Borg CR10 RPE scale of the participants should not exceed 7. If the participants could successfully complete the first stage of the exercise training, they would proceed to the next stage of exercise, and the training would be further upgraded to assisting the participants to sit at the bedside in an upright posture and perform sitting balance training. The physical therapists would provide minimal assistance or assistive devices according to the participants' conditions. The goal was to achieve tolerance for 20 min continuously with the modified Borg CR10 RPE scale not exceeding 7 and no contraindication. In the third stage, the physical therapists would adopt appropriate strategies and assistive devices according to the participants' abilities and move the participants to chairs. The fourth stage was standing training. The participants could use assistive devices or other assistance to stand. The fifth stage was marching on spot. All exercise training were guided by the principle of maximum active participation of participants, with the goal of continuous completion of body movements and spontaneous breathing movements.

Termination conditions of continuous mobility training: The training would be terminated immediately if the participants had the following conditions: Unstable vital signs: low blood oxygen concentration (SaO_2 ≤90%) or shortness of breath (total respiratory rate >35 bpm); arrhythmia; severe dizziness; changes in consciousness; assessment by attending physician that the participant's condition, progression of disease course or treatment plan was not suitable for activities of exercise therapy.

After the intervention, the length of mechanical ventilation, length of stay in the respiratory care center, the success rate of mechanical ventilation weaning (weaning for more than five days), the total length of hospital stay, and adverse events of two groups were recorded with evaluator-blind.

Statistical analysis

All participants were included in the intention-to-treat analysis. Statistical analysis was performed using the IBM SPSS version 27.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. Comparative analysis between the experimental group and the control group was performed according to all the effect variables. The evaluation records of the two groups of participants were compared. All of the continuous variables conformed to normal distribution after Shapiro-Wilk test and were compared by two sample independent t-test. The chi-square test was used to evaluate the differences in the categorical variables between the experimental group and the control group. To calculate the sample size for duration of mechanical ventilation, we based the design on results found in Lai et al.[20] for a clinical trial. Considering a statistical power of 90% and alpha error of 0.5, we found that the number of subjects should be 9 per group, totaling 18 participants. A p value of <0.05 was considered statistically significant.

RESULTS

There were 56 participants who were randomly and equally assigned to the experimental group and control group. Three participants in the experimental group and two participants in the control group were transferred back to the ICU due to changes in their disease conditions. Effect analysis was conducted in 28 participants in the experimental group and 28 participants in the control group.

Table 1 shows the demographic characteristics of both groups. The mean length of stay at the ICU was 24.3±12.0 days. There was no significant difference in demographic characteristics between the two groups (p>0.05).

TABLE 1
Demographic and clinical variables of the groups at the time of admission

Variables	All (n=56)			Intervention (n=28)			Control (n=28)			*p*
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
Age (year)			70.1±15.9			66.7±17.0			73.5±14.2	0.110
Sex										
Male	33	58.9		18	64.3		15	53.6		0.415
Height (cm)			159.0±9.0			161.0±8.0			158.0±10.0	0.188
Body weight (kg)			59.3±15.7			61.9±18.1			56.7±12.6	0.215
Body mass index (kg/m^2)			23.2±4.7			23.8±5.7			22.6±3.5	0.373
ICU										0.778
MICU	37	66.1		18	64.3		19	67.9		
SICU	19	33.9		10	35.7		9	32.1		
ICU (day)			24.3±12.0			23.8±11.5			24.8±12.7	0.767
Underlying comorbidity										
Pneumonia	29	51.8		13	46.4		16	57.1		0.422
COPD	9	16.1		4	14.3		5	17.9		0.716
Stroke	10	17.9		4	14.3		6	21.4		0.485
Craniotomy	12	21.4		5	17.9		7	25.0		0.515
Spinal cord injury	3	5.4		2	7.1		1	3.6		0.553
CAD	16	28.6		6	21.4		10	35.7		0.237
Congestive HF	5	8.9		2	7.1		3	10.7		0.639
Diabetes	25	44.6		12	42.9		13	46.4		0.788
Hypertension	28	50.0		12	42.9		16	57.1		0.285
CRF-hemodialysis	15	26.8		7	25.0		8	28.6		0.763
MV mode										0.145
Pressure control	24	42.9		12	42.9		12	42.9		
SIMV + pressure control	9	16.1		2	7.1		7	25.0		
Pressure support	23	41.1		14	50.0		9	32.1		

SD: Standard deviation; ICU: Intensive care unit; MICU: Medical intensive care unit; SICU: Surgical intensive care unit; COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease; HF: Heart failure; CRF: Chronic renal failure; MV: Mechanical ventilator; SIMV: Synchronized intermittent mandatory ventilation; * p<0.05.

Table 2 shows the analysis of the test values and mechanical ventilator values of the participants. There was no significant difference in test values or mechanical ventilator values between the two groups (p>0.05).

Table 3 shows the clinical effect analysis of the participants. The success rate of mechanical ventilation weaning in the experimental group was higher than that in the control group (89.3% *vs.* 67.9%), but there was no statistically significant difference (p=0.051). Compared to the control group, the mean length of mechanical ventilation of the experimental group was shorter (17.1±10.5 *vs.* 29.0±13.4 days, p=0.000), and the mean length of stay at the respiratory care center was also shorter (21.5±9.6 *vs.* 34.8±14.6 days, p=0.000), with statistically significant differences. The mean length of hospital stay of the experimental group and the control group were 59.3±21.5 and 70.5±24.4 days, respectively, and there was no significant difference between the two groups (p=0.075). During the training period, there was no adverse event, such as blood oxygen reduction, occurred in either group.

DISCUSSION

In the present study, we examined the clinical effects of the continuous mobility training in participants with prolonged mechanical ventilation. In participants with prolonged mechanical ventilation, multi-mode rehabilitation exercises, including muscle strength training, endurance training, and functional retraining, could increase the success rate of mechanical ventilation weaning (87% *vs.* 41%, p<0.01).[21] In addition, using endurance training to change the performance of the diaphragm muscle and increasing the length of physical therapy intervention were all directions of early activity content design.[22,23] The content of the continuous mobility training designed in this study was based

TABLE 2
Laboratory and ventilator data of the groups at the time of admission

Variables	All (n=56) Mean±SD	Intervention (n=28) Mean±SD	Control (n=28) Mean±SD	*p*
Blood urea nitrogen level (mg/dL)	37.5±26.4	31.2±23.6	43.8±27.9	0.075
Creatinine level (mg/dL)	1.6±1.8	1.5±1.7	1.8±1.7	0.632
Sodium level (mmol/L)	136.5±4.8	136.0±4.1	137.1±5.6	0.443
Potassium level (mmol/L)	3.9±0.5	3.9±0.4	3.9±0.6	0.837
HCO_3 (mmol/L)	25.4±5.1	25.9±4.4	24.9±5.8	0.442
pH	7.424±0.070	7.418±0.071	7.430±0.070	0.515
PaO_2 (mmHg)	133.2±62.8	122.4±41.9	143.9±77.6	0.201
$PaCO_2$ (mmHg)	40.0±9.6	41.1±8.2	38.9±10.8	0.386
Hemoglobin level (g/dL)	10.6±1.3	10.5±1.1	10.7±1.5	0.599
Hematocrit level (g/dL)	32.1±3.6	32.1±2.8	32.1±4.5	0.966
SBP (mmHg)	136.6±23.2	141.0±24.3	132.2±21.6	0.156
DBP (mmHg)	72.5±14.7	76.1±15.0	68.8±13.6	0.059
Heart rate (beats/min)	78.8±14.7	79.5±15.3	78.2±14.5	0.747
Respiratory rate (breaths/min)	26.8±6.7	25.6±6.4	28.0±6.8	0.182
FiO_2	29.4±3.4	29.6±3.3	29.1±3.6	0.566
Tidal volume (mL)	308.4±114.5	331.3±122.5	285.5±103.0	0.136
Minute ventilation (L/min)	8.0±3.2	8.3±3.4	7.8±3.1	0.497
PEEP (mmHg)	6.5±1.0	6.7±1.0	6.4±1.1	0.302
MIP (mmHg)	-38.3±15.6	-40.2±15.4	-36.4±15.8	0.368
MEP (mmHg)	37.3±17.4	38.9±20.4	35.6±14.1	0.476
RSBI	99.2±44.0	91.3±45.5	107.1±41.7	0.180

SD: Standard deviation; PaO_2: Partial pressure of oxygen, arterial; $PaCO_2$: Partial pressure of carbon dioxide, arterial; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FiO_2: Fraction of inspired oxygen; PEEP: Positive end expiratory pressure; MIP: Maximal inspiration pressure; MEP: Maximal expiration pressure; RSBI: Rapid shallow breathing index; * p<0.050.

TABLE 3
Differences in the clinical effects between the two groups

Variables	All (n=56) n	%	Mean±SD	Intervention (n=28) n	%	Mean±SD	Control (n=28) n	%	Mean±SD	*p*
MV (day)			23.1±13.3			17.1±10.5			29.0±13.4	0.000*
RCC (day)			28.1±14.0			21.5±9.6			34.8±14.6	0.000*
Length of hospital stay (day)			64.9±23.5			59.3±21.5			70.5±24.4	0.075
Weaning success	44	78.6		25	89.3		19	67.9		0.051

SD: Standard deviation; MV: Mechanical ventilator; RCC: Respiratory care center; * p<0.05.

on the duration of physical mobility, which allows the participants to perform physical mobility and spontaneous breathing movement. The goals of the continuous mobility training designed in this study aimed at enduring the training for 20 min continuously and promoting endurance performance of the trunk muscles and the diaphragm muscle. The results of this study showed that for participants with prolonged mechanical ventilation, continuous mobility training could reduce length of mechanical ventilation and the length of stay at the respiratory care center. The reducing the length of mechanical ventilation and staying in the respiratory care center could both effectively reduce medical resource consumption. The mechanical ventilation weaning rate of the experimental group was higher than

that of the control group; however, there was no statistically significant difference. There was no significant difference in the total length of hospital stay between the two groups. Besides prolonged mechanical ventilation, most participants in this study had other diseases, and the total length of hospital stay may have been affected by the treatment of other diseases.

Adverse events were recorded continuously during the study, and there were no adverse events, such as blood oxygen reduction, in both groups, which showed that the continuous mobility training of participants using mechanical ventilation was safe and effective provided that the enrollment criteria and the safety monitoring strategy for implementing the training were complete.

Many published articles have confirmed the effect of early exercise on participants using mechanical ventilation, and the exercise protocol has its diversity, which warrants further investigation.[24,25] In clinical practice, the implementation of early rehabilitation for participants using a mechanical ventilation is not as common as expected.[26,27] According to research statistics from Germany, only 24% of participants who used mechanical ventilation and 8% of participants who used endotracheal tubes would set out-of-bed activities as a part of routine care.[28] Therefore, early exercise intervention of participants using mechanical ventilation needs continuous research and exploration to form a clinical pathway.[29,30]

The team members and families must participate together for participants with prolonged mechanical ventilation.[31,32] Exercise training studies in participants with prolonged mechanical ventilation have been conducted. Six-week training of respiratory muscles and limb muscles could promote limb muscle strength, shorten mechanical ventilation-free time, and improve physical function.[33] Another study showed that participants with prolonged mechanical ventilation participated in physical therapy training under monitoring for six weeks and the scores of motor domain and cognitive domain increased significantly.[34,35] In participants with difficulty in weaning from the mechanical ventilation, active rehabilitation training of peripheral muscles was performed every day, and the daily living function was improved, which would make the mechanical ventilation weaning success rate different.[36] In general, if the patient's daily life function improves, it signifies the improvement in body movement function, as well as respiratory and circulatory system ability. Aggressive whole-body rehabilitation and respiratory muscle training for participants with prolonged mechanical ventilation would improve their muscle strength, mechanical ventilation weaning effect and functional status.[37]

Nonetheless, there are several limitations to this study. The individuals who implemented exercise training and participants who received exercise training could not be blinded, which may have led to deviation. Moreover, this study was conducted in a single center; therefore, the research results cannot fully represent other respiratory training centers. Finally, there are great differences in disease categories among the participants who received training for mechanical ventilation weaning in the respiratory care center. Different disease categories would have an impact on the setting of mechanical ventilation and body movement function.

In conclusion, the continuous mobility training for participants with prolonged mechanical ventilation can reduce the length of mechanical ventilation and stay at the respiratory care center; however, it has no significant effect on the success rate of mechanical ventilation weaning and the total length of hospital stay. Further large-scale, prospective studies are needed to confirm these findings.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, literature review, writing the article, references and fundings, control/supervision: C.W.L.; Data collection and/or processing: C.W.H.; Analysis and/or interpretation, critical review: Y.H.C.; Materials: C.M.L.

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