Comparison of the effects of intermittent weight bearing and short duration stretching on disuse atrophy of rat soleus muscles

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# Comparison of the effects of intermittent weight bearing and short duration stretching on disuse atrophy of rat soleus muscles

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#### ABSTRACT

The present study was undertaken to examine whether or not there would be any differences in the effect of suppressing muscular atrophy between intermittent weight bearing and short duration stretching applied with controlled timing and frequency during progressive disuse atrophy. Experimental materials selected were the soleus muscles of male Wistar rats. The rats were divided into the control group and the experimental group. The experimental group was subdivided into three groups: hindlimb suspension(HS)-only group, HS+intermittent weight bearing group, and HS+short duration stretching group. Weight bearing was induced by temporarily removing the suspension. The right soleus in the STR group was maximally stretched by dorsiflexing the ankle joint with non-elastic tape. Weight bearing and stretching was performed daily for one hour. The study period was set at 2 weeks.

Short duration stretching suppressed muscular atrophy when the cross sectional area of muscle fibers was analyzed as an indicator of atrophy. However, it exerted no evident qualitative effects. Intermittent weight bearing had effects on all of the muscular weight, fiber composition and cross sectional area. Under the conditions used in this study, intermittent weight bearing was more useful in suppressing the progression of disuse atrophy of muscles than short duration stretching.

## KEY WORDS

intermittent weight bearing, short duration stretching, disuse atrophy, soleus muscle, rat

# Introduction

Skeletal muscles of the lower extremities tend to atrophy if people remain inactive in bed for prolonged periods or if their muscles are kept from weight bearing, as in after surgery. This is called "disuse atrophy" and it has been shown to be relatively reversible. Since the lack of weight bearing is the cause of disuse atrophy, resumption of weight bearing is considered an appropriate clinical countermeasure for dealing with this condition 1.2). However, depending on the patient's condition and/or the length of the non-weight bearing period, it is often difficult

to resume adequate functional weight bearing activity In cases where no weight bearing is permitted at all measures such as isometric contraction and passive muscular stretching are undertaken with instruction by a physical therapist<sup>3</sup>. Often a physical therapis supervises these measures on the basis of empirica knowledge while monitoring the patient closely. It such cases, an explanation of the method of treatmer and the reasoning should be given to the patient.

The condition called "disuse atrophy of muscle has been reported by many investigators, includin those who have studied the adaptation of astronauts

the micro-gravitational environment of space and looked for countermeasures to take when the astronauts return to earth 4-9). Pathological changes associated with disuse atrophy have been studied in depth. using animal models in hindlimb suspension 10, 111. Muscular atrophy induced by hindlimb suspension resembles muscular atrophy observed among bedridden individuals in hospitals and institutions. The authors therefore studied the effects of intermittent weight bearing<sup>12-14)</sup> and short duration stretchin g3,15-17) of muscles (performed under varying conditions) upon the suppression of the progress of muscular atrophy using this animal model. This past study has revealed that timing and frequency are important factors. We came to the conclusion that clinical efficacy at suppressing the progress of muscular atrophy is greater when using intermittent weight bearing than when using short duration stretching. To date, however, no report has clearly revealed differences in efficacy between these two methods.

The present study was undertaken to examine whether or not there would be any differences in the effect of suppressing muscular atrophy between intermittent weight bearing and short duration stretching applied with controlled timing and frequency during progressive disuse atrophy.

#### Methods

Experimental materials selected were the soleus muscles of male Wistar rats (n=18, body weight;  $217\pm8\,\mathrm{g}$ ). This study was conducted pursuant to the guidelines for the care and use of laboratory animals in Takara-machi Campus of Kanazawa University. Disuse atrophy of muscle was induced by hindlimb suspension using the device described in our previous study<sup>18)</sup>. The study period was set at 2 weeks.

The rats were divided into the control group (CON) and the experimental group. The experimental group was subdivided into three groups: hindlimb suspension-only group (HS), HS+intermittent weight bearing group (WB), and HS+short duration stretching group (STR). Weight bearing was induced by temporarily removing the suspension. The right soleus in the STR group was maximally stretched by dorsiflexing the ankle joint with non-elastic tape<sup>3)</sup>. In the WB, STR and CON groups, the right soleus was the subject of

the experiment, and in the HS group, the left soleus in this study. Weight bearing and stretching was performed daily for one hour.

After body and muscle weight were measured, the muscles were stored at  $-80\,^{\circ}\text{C}$  until histochemical analysis. Later transverse sections were prepared and classified as to muscle fiber type (I and II) by ATPase staining. The cross sectional area of more than 100 muscle fibers in each muscle was measured as described in a previous study<sup>18)</sup>. The proportion of each type was also calculated.

For the statistical evaluation of differences among groups, a one-way analysis of variance was performed, followed by Scheffe's post hoc test (P<0.05). Data were expressed as mean $\pm$ SD.

# Results

Compared with the CON, the wet weight of soleus muscle in the experimental group was significantly smaller. Among the experimental groups, the parameter in the WB group was significantly greater than that in the HS group. But no statistically significant difference was observed between the other experimental groups. The relative weight in the HS and STR group was significantly smaller than that in the CON group. Among the experimental groups, the relative weight in the WB group was significantly greater than that in the HS group (Table 1).

The proportion of type I fibers in the experimental groups tended to decrease compared with the CON group. Among the experimental groups, type I fibers in the WB group were significantly greater than those in the HS group (Table 1).

The mean cross sectional area of type I fibers in the WB group decreased to 68.6%, in the STR group to 54.2%, and in the HS group to 49.4% of the value for the CON group. A statistically significant difference was recognized between all groups (Fig. 1). Figures 2 and 3 show in graphical form the distribution of the cross sectional area of all measured fibers. For type I fibers, the distribution in the experimental group was shifted to the left side of that in the CON group and the range of distribution was also narrow. The WB group was located between the HS and CON group. The STR group showed a similar distribution to the HS group, but the peak value was lower

Table	1.	Muscle	mass	and	proportion	of	fiber	types.

	Muscle weight	Relative weight	Proportion		
	(mg)	(mg/g)	Type I (%)	Type II (%)	
CON	108±9†	0.37±0.03†	73.7±1.7†	26.3±1.7†	
WB	67±5*†	$0.33 \pm 0.03 \dagger$	68.1±1.7*†	$31.9 \pm 1.7 * †$	
STR	56±8*	0.28±0.03*	66.3±2.2*	33.7±2.2*	
HS	50±8*	0.25±0.03*	63.9±2.5*	36.1±2.5*	

Relative weight = muscle weight/body weight, \*: p<0.05 (compared with CON), †: p<0.05 (compared with HS).

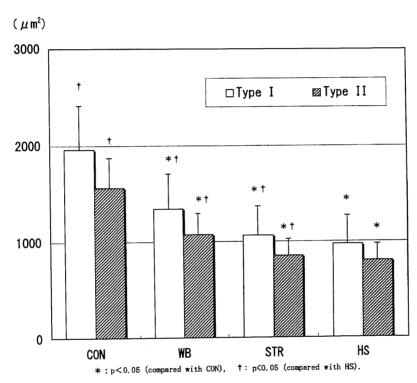


Fig. 1 Cross-sectional area of soleus muscle fibers.

than that in the HS group (Fig. 2). The mean cross sectional area of type II fibers in the WB group decreased to 68.8%, in the STR group to 54.5%, and in the HS group to 51.1% of the value for the CON group. A statistically significant difference was recognized between all groups (Fig. 1). Type II fibers also showed a similar distribution to type I fibers, but the peak value of type II fibers in the STR group was higher than that in the HS group (Fig. 3).

#### Discussion

In the present study, the effect in suppressing the progression of disuse atrophy of muscles was compared between two clinical methods (intermittent weight bearing and short duration stretching), using rat soleus muscles. The relative weight in the WB group did not differ from that in the CON group, indicating that progression of atrophy was prevented by one-hour weight bearing per day. The wet weight of the muscle was also significantly greater in the

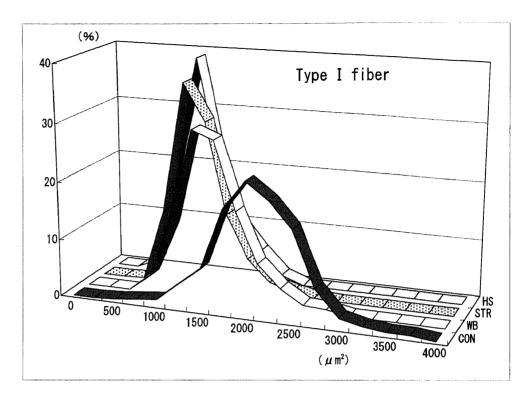


Fig. 2 Size distribution of type I fibers.

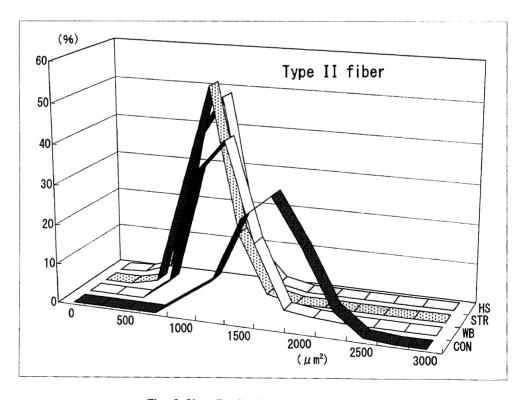


Fig. 3 Size distribution of type II fibers.

WB group than in the HS group, indicating the efficacy of weight bearing. However, it did not differ between the STR and HS groups. Thus, stretching had no effect on muscular weight. When the proportion of each type of muscle fiber was analyzed, the experimental groups showed a tendency for an increase in type II fibers. The percentage of type I fiber was significantly higher in the WB group than in the HS group, indicating the efficacy of weight bearing. In the STR group, neither muscular weight nor the percentage of type I fiber showed any difference from the HS group. Stretching had neither quantitative nor qualitative effects. The cross sectional area of both t ype I and II muscle fibers changed following weight bearing or stretching. This parameter was significantly higher in the WB group than in the STR group, indicating greater efficacy with weight bearing than with stretching. However, it was not possible to completely prevent a decrease in cross sectional area of muscle fibers (atrophy) by one-hour intervention per day. Thus, short duration stretching suppressed muscular atrophy when the cross sectional area of muscle fibers was analyzed as an indicator of atrophy. However, it exerted no evident qualitative effects, i.e., no evident effects on muscular weight or the composition of muscle fibers (a qualitative aspect). Intermittent weight bearing had effects on all of the muscular weight, fiber composition and cross sectional area. Thus, intermittent weight bearing seems to be more useful in suppressing atrophy than stretching.

We previously reported the effects of anesthesia on the efficacy of short duration stretching<sup>3,17)</sup>. In the present study, stretching was performed in unanesthetized animals. It seems likely that stretching induced stimulation of muscles as well as suppression of muscular atrophy due to resistance of the rat to the manipulation. The ankle joint position of plantarflexion, which is seen in long-term bed-ridden patients, is also seen in rats during hindlimb suspension. According to Riley et al.19, the ankle joint of rats during quiet weight bearing shows an approximately 60-degree dorsi-flexion, but hindlimb suspension gradually induces plantar-flexion, leading to shortening of the soleus muscle and a decrease of the range of motion to 0 degree (dorsi-flexion) - 90 degrees (plantar-flexion). Ohira et al.201 reported that the length of the soleus muscle during hindlimb suspen sion is about 10 mm shorter than that during quie weight bearing. Passive stretching of the soleu muscle under this condition is expected to suppres atrophy. Intermittent weight bearing seems to stimu late an increase in muscular work by inducing stretch ing of the soleus muscle and supporting the bod weight. This is probably the greatest factor explaining the finding that intermittent weight bearing produce more suppression of atrophy than did short duration stretching. Also during hindlimb suspension, activ movement of the ankle joint is possible. Although th electromyographic activity decreases immediately afte suspension, it normalizes in 7 days in the case of th soleus muscle<sup>20)</sup>. A problem with this effect is that i is not accompanied by manifestation of muscula tension. It appears that normal muscular activity doe not take place during non-weight bearing, leading t a decrease in afferent information transmission fror muscles to the central nervous system and an inabilit to retain normal muscular functioning. In this respecweight bearing seems to be more favorable.

Under the conditions used in this study, intermitter weight bearing was more useful in suppressing th progression of disuse atrophy of muscles than shorduration stretching. However, since the respons differed among different types of muscle fibers, it is required for us to devise various countermeasure depending on the type of muscle fibers. There are many clinical cases where weight bearing is difficult due to the duration of the non-weight bearing period or other factors. In such cases, stretching with appropriate timing and frequency will be a more effective physical therapy.

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# ラットヒラメ筋の廃用性萎縮に及ぼす間欠的荷重 および短時間伸張位保持効果の比較

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# 要 旨

本研究では廃用性筋萎縮の進行中に、時間および頻度を規定した状態で、間欠的に荷重または伸張位保持を実施し、その萎縮抑制効果に相違があるか否かを検索した。Wistar 系雄ラットのヒラメ筋を対象筋とした。ラットを対照群と実験群に分けた。実験群は、後肢懸垂群、後肢懸垂中に間欠的に荷重する群、および後肢懸垂中に伸張位保持を実施する群の3群とした。荷重は、懸垂用装具をはずした四肢荷重状態とし、終了後は再び懸垂した。伸張位保持は、懸垂中ラットの右足関節を非伸縮性テープで最大背屈位に固定することで、ヒラメ筋を伸張した。荷重および伸張位保持は1日1時間とし、毎日実施した。実験期間は2週間に設定した。

その結果、伸張位保持は筋線維断面積において萎縮抑制効果を示したが、質的影響は明らかではなかった。間欠的荷重では、筋重量、タイプ構成比率および断面積において介入効果が認められた。断面積は伸張位保持群より荷重群で有意に大きかった。以上より、廃用性筋萎縮の進行抑制に関しては、間欠的荷重が短時間伸張位保持より効果的であることが示唆された。