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2

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4 swelling in healthy young men

5

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20

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ABSTRACT

29 The effects of high-loaded resistance training on muscle strength and muscle mass depend on
30 rest periods between sets. However, whether differences in rest periods during low-loaded
31 resistance exercise (RE) have an influence on improving muscle characteristics remains unclear.
32 Understanding the effects may guide to prescribe low-loaded resistance exercise safely and
33 effectivity. The purpose of this study was to investigate acute effects of low-loaded RE on
34 muscle swelling with different rest periods between sets. A total of 42 young men (age,
35 22.9 ± 2.4 years; height, 172.1 ± 5.4 cm; body mass, 65.6 ± 6.5 kg) were recruited to participate in
36 the study. They were assigned to one of three groups with different rest periods between sets
37 (20 s, 60 s, or 180 s). A total of 12 sets of 10 repetitions of RE with 30% of one repetition
38 maximum on knee extensor muscles were performed. Muscle thickness of the vastus lateralis
39 was measured using ultrasonography as indicator of muscle swelling every 3 sets. Muscle
40 thickness significantly increased after 3 sets of RE in the 20-s ($3.9 \pm 3.3\%$) and 60-s groups
41 ($5.9 \pm 3.8\%$) but only after 12 sets in the 180-s group ($4.3 \pm 3.1\%$). REs with rest periods shorter
42 than 60 s could result in exercise-induced muscle swelling after fewer sets of RE.

43 **Key words:** knee extensors; ultrasound; muscle swelling; rest interval

44

45 **表題：**低強度筋力トレーニングにおける休息時間の違いが運動直後の一過性の筋厚変化に及ぼす

46 影響

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53 **Abstract:**

54 本研究の目的は、低強度筋力トレーニングにおいてセット間の休息時間が即時的な筋厚変化に
55 及ぼす影響を検証することである。対象は健常若年男性 42 名とし、セット間休息時間の異なる 3
56 群(20 秒群，60 秒群，180 秒群)に無作為に分類した。30%1RM の低強度での膝伸展筋力トレーニ
57 ングを 10 回 1 セットとして 12 セット施行した。超音波診断装置を用いて外側広筋の筋厚を運動
58 開始直前と 3 セット，6 セット，9 セット，12 セット終了時に計測した。なお，運動直後の筋厚
59 の増加はトレーニングによる代謝物蓄積による浸透圧変化による一過性の水分貯留の結果であ
60 る。その結果，20 秒群と 60 秒群は 3 セット終了以降で運動直前に対して有意な筋厚の増加を認
61 めた。一方，180 秒群では 12 セット終了時のみ有意な筋厚の増加を認めた。12 セット終了時の筋
62 厚変化率には 3 群間で有意差はみられなかった。本研究の結果から，低強度筋力トレーニングに
63 においてセット間休息時間が短いと早期から一過性の筋厚増大が生じることが示唆された。

INTRODUCTION

64

65 Resistance exercise (RE) promotes health benefits and is generally prescribed as an
66 intervention to increase muscle mass in patients with neuromuscular diseases, musculoskeletal
67 disease, disuse, and aging.¹ Conventionally, RE with high load, such as 60–80% one repetition
68 maximum (1RM), for >6 weeks has been suggested to generate muscle hypertrophy.^{2,3} It has
69 been reported that high-loaded resistance training causes muscle hypertrophy in older adults⁴.
70 However, high-loaded RE is also known to be associated with some risk factors causing
71 orthopedic injury⁵ as well as can increase the heart rate and blood pressure excessively⁶.
72 Therefore, especially for frail, older adults or patients, low-loaded RE is often prescribed. Some
73 studies have demonstrated that even low-loaded RE could result in muscle strengthening and
74 change the muscle morphology^{7–13}.

75 The effects of RE are influenced by contraction mode, loading volume, repetition
76 velocity, and rest period between sets.^{2,14–18} A recent study reported that RE could have similar
77 effects of muscle hypertrophy if the training volume (the accumulation of absolute work) was
78 of the same condition, even when the contraction mode was different (i.e., concentric versus
79 eccentric contractions), as long as total absolute mechanical work was equal.¹⁹ Mitchell, et al.⁸
80 or Ikezoe, et al.⁷ reported that even at the low-loaded RE of 30% 1RM, high-repetition
81 resistance training to volitional failure resulted in the same effect on muscle hypertrophy as did
82 resistance training at a high-loaded RE of 80% 1RM. Tanimoto and Ishii¹⁰ reported that when

83 exercises are performed with slow sustained muscular contraction, low-loaded RE of 50% 1RM
84 result in the same effect on muscle hypertrophy as high-intensity RE of 80% 1RM. Thus, even
85 low-loaded RE has been considered to exert the same effects on muscle hypertrophy as high-
86 loaded training by increasing the number of repetitions or performing with sustained muscular
87 contraction.

88 In addition, rest periods between sets of resistance training, which associate with
89 metabolic stress, have been considered to affect muscle hypertrophy.¹⁶ With regard to the
90 effects of rest periods between sets, Villanueva, et al.²⁰ reported that high-loaded resistance
91 training for 8 weeks with 60-s rest periods elicited greater improvements in body composition,
92 muscular performance, and functional performance compared to those with 4-min rest periods
93 among older adults. On the other hand, de Salles, et al.²¹ showed that high-loaded resistance
94 training with 3- or 5-min rest periods caused greater improvements in muscle strength than
95 training with 1-min rest periods, when resistance training is performed to failure. Since
96 resistance training with longer rest periods might lead to increase in the number of repetitions,
97 i.e., increase in training volume, greater improvements in muscle strength may be explained by
98 the high training volume. In other words, Villanueva, et al.²⁰ and de Salles, et al.²¹ demonstrated
99 that differences were observed in the effects of high-loaded resistance training on muscle
100 strength and muscle mass depending on rest periods between sets. However, whether
101 differences in rest periods during low-loaded RE have an influence on improving muscle

102 characteristics remains unclear.

103 Several studies using ultrasonography or MRI have reported that muscle thickness or
104 cross-sectional area (CSA) increases immediately after one session of RE.²²⁻²⁵ The acute
105 effects on muscle thickness and CSA, which itself is not muscle hypertrophy, have been
106 considered to be an important factor to induce muscle hypertrophy.^{17,26} The increase in muscle
107 thickness or CSA, that is, muscle swelling following RE, has been recognized to be due to
108 alterations in intra- and extracellular water balance induced by increased vascular
109 permeability.²⁷ With regard to vascular permeability, RE may cause cellular accumulation of
110 lactate and hydrogen ions, which are induced by degradation of muscle glycogen.²⁸ The
111 molecular weights of lactate and hydrogen ions are smaller than that of muscle glycogen.
112 Therefore, the high lactate and hydrogen ion concentrations and concomitant increase in
113 intracellular acidosis after exercise²⁹ may accelerate water uptake in muscle cells according to
114 permeability.³⁰⁻³² Increased pressure against the cell membrane causes activation of anabolic
115 protein kinase transduction pathways, which can subsequently promote muscle hypertrophy.³³⁻
116 ³⁵ Fahs³⁶ has shown that RE without blood flow restriction to failure can generate acute effects
117 on muscle swelling similar to that observed in RE with blood flow restriction. Moreover, same
118 muscle hypertrophy effects between the two RE groups have been observed after a 6-week
119 intervention. These studies suggest that muscle swelling such as an increase in muscle
120 thickness immediately after RE could possibly be associated with muscle hypertrophy after

140 (G*Power 3.1, Dusseldorf, Germany). We conducted a pilot study with seven participants to
141 evaluate the effect size for the main variable, which indicated that the effect size was large.
142 According to the large effect size, the power analysis using an effect size of 0.40, an α error of
143 0.05, and a power of 0.80 revealed that the required sample size was 14 subjects for each group.
144 Because the acute effects of exercise are often attenuated when subsequent bouts of similar
145 exercise are performed (called “repeated bout effect”),^{37,38} the acute effect on muscle thickness
146 may be acclimatized after the second or third session of RE. Therefore, we allocated the
147 participants among three groups, and compared the acute effect after the first bout of RE in
148 each group.

149 All participants were sufficiently informed about the purpose of this study, and signed
150 written consent was obtained prior to the start of the study. The study was approved by Kyoto
151 University Graduate School of Medicine Ethics Committee (E2246) and conducted in
152 accordance with the Declaration of Helsinki.

153

154 Resistance Exercise

155

156 The participants were assigned to three groups with different rest periods between sets: 60 s as
157 the basic rest period, 20 s as a group with a shorter rest period, or 180 s as a group with a longer
158 rest period.

159 RE was performed using ankle cuff weights at the distal lower leg, which is usually
160 used as low-loaded resistance exercise. The participants were seated without their feet touching
161 the floor. The RE for knee extensors on the right leg consisting of 12 sets with 10 repetitions
162 was performed with each rest period, based on our previous study ⁷. Both concentric and
163 eccentric contractions for 3 s through the entire range of motion of the knee (90° – 0° ; 0° = full
164 knee extension) and isometric contraction at 0° for 1 s in between concentric and eccentric
165 contraction were performed, based on a previous study¹³. The movement speed was regulated
166 with the aid of a metronome at 60 rpm. The participants were instructed not to accelerate
167 quickly.

168 RE load was set at 30% of 1RM, based on the value of 1RM measurement. The 1RM
169 was measured by increasing the load every 10 Nm, using the isotonic mode of a dynamometer
170 (Biodex System 4, Biodex Medical Systems, Shirley, NY, USA). The definition of 1RM was
171 the maximum load that the participants could produce against the set load in order to move
172 their leg through a range of motion one time (90° – 0° ; 0° = full knee extension). The 1RM
173 measurement with 2-min rest between each trial was performed after a warm-up session of 10–
174 20 submaximal contractions. The 1RM measurement was performed more than 3 days prior to
175 the RE not to affect the ultrasound measurements.

176

177 Measurements of muscle swelling

178

179 Muscle thickness of the vastus lateralis obtained using transverse ultrasound images was used
180 as an indicator of muscle swelling.³⁶ Muscle thickness was measured using B-mode ultrasound
181 imaging device (LOGIQ e, GE Healthcare UK, Chalfont, UK) with an 8 MHz linear array
182 probe (58 dB gain) before (pre-exercise) and after 3 sets, 6 sets, 9 sets, and 12 sets of RE. The
183 participants were positioned in a sitting position with 90° hip and knee flexion and were
184 instructed to be relaxed without muscle contraction during measurement. The transducer was
185 placed at two-thirds on the line from the anterior spina iliaca superior (ASIS) to the lateral side
186 of the patella without interlapping an electromyography (EMG) sensor (just distal from the
187 sensor). All measurements were performed by the same investigator who has established his
188 own intersession reliability.

189

190 Measurement of muscle activity during RE

191

192 The muscle activity of the vastus lateralis during RE was recorded via surface EMG
193 (TeleMyo™ 2400T DTS, Noraxon Inc., Scottsdale, Arizona, USA) with 1500 Hz of sampling
194 frequency. Surface EMG electrodes (Blue sensor M-00-S/50, AMBU, Ballerup, Denmark) with
195 a 20 mm center-to-center interelectrode distance were placed at two-thirds on the line from the
196 ASIS to the lateral side of the patella according to the recommendations of the Surface

197 Electromyography for the Non-Invasive Assessment of Muscles project.³⁹ The raw EMG
198 signals were processed using a bandpass filter between 20 and 500 Hz. The EMG activity was
199 rectified using a root mean square (RMS) algorithm and was expressed as a percentage of the
200 maximum voluntary isometric contraction (MVIC) for knee extension at 90° knee flexion. The
201 muscle activity was averaged every 3 sets during RE.

202

203 Intersession reliability of the measurements

204

205 To determine intersession reliabilities of the measurements of muscle thickness for the vastus
206 lateralis, measurement was performed twice in eight healthy young men (age: 22.4±0.9 years).
207 The intraclass correlation coefficient (ICC [1.1]) for the measurements of muscle thickness was
208 0.986.

209

210 Statistical analyses

211

212 Statistical analyses were performed using SPSS version 22.0 software (IBM Japan, Inc., Tokyo,
213 Japan). Shapiro-Wilk test was employed the normality of the data. When the normality was not
214 achieved, Friedman test was used to analyze changes in muscle thickness followed by RE every
215 3 sets in each group. When a significant main effect was observed, Wilcoxon's tests with

216 Bonferroni correction were performed to determine where the difference occurred relative to
217 pre-exercise. Additionally, effect size (ES) was calculated for each sets compared to pre-
218 exercise. The percentage changes in muscle thickness after 3, 6, 9, and 12 sets of RE were
219 calculated as follows: percent change = (after RE – pre-exercise)/pre-exercise. The differences
220 in the percentage changes in muscle thickness after 3, 6, 9, and 12 sets of RE were assessed
221 between the groups using Kruskal-Wallis test. One-way repeated-measures analysis of variance
222 (ANOVA) was performed to compare time-course of muscle activities during every 3 sets
223 normalized to MVIC in each group. When a significant main effect was observed, Bonferroni
224 post-hoc tests were used to examine differences between sets. Statistical significance was set
225 at an alpha-level of 0.05.

226

227

RESULTS

228

229 Table 1 shows the participants' baseline characteristics, 1RM, and weights during RE. No
230 differences were observed for their age, height, body mass, 1RM, and weight among the three
231 groups.

232

233 Changes in muscle thickness

234

235 Table 2 shows the muscle thickness measured before and after every 3 sets of RE in each group.
236 The Friedman tests indicated main effects for time in all groups (all groups; $p < 0.01$). In the 20-
237 s and 60-s groups, the post-hoc analysis showed a significant improvement in muscle thickness
238 at 3 sets. In the 180-s group, a significant increase in muscle thickness was observed only after
239 12 sets of RE.

240 The percentage change values in muscle thickness after 3, 6, 9, and 12 sets of exercise
241 are shown in Table 2. The Kruskal-Wallis tests revealed that no significant differences were
242 found in the percentage change between the groups in each 3 sets (after 3 sets of exercise; $p =$
243 0.117, after 6 sets of exercise; $p = 0.068$, after 9 sets of exercise; $p = 0.080$, after 12 sets of
244 exercise; $p = 0.152$).

245 (Table 2 about here)

246

247

248 Muscle activity during RE

249

250 Figure 1 shows the muscle activity (%MVIC) for each of the 3 sets. The ANOVAs indicated
251 main effects for time in the 20-s and 60-s groups. However, no main effect was observed in the
252 180-s group. The post-hoc test revealed that muscle activity during 10–12 sets was significantly
253 greater than during 1-3, 4–6 and 7–9 sets both in the 20-s and 60-s groups.

254

255

DISCUSSION

256

257 This study compared the acute effect of low-loaded RE on muscle swelling among three
258 exercises conditions with the same muscle contraction time and different rest periods. The
259 results revealed that the increase in muscle thickness was observed after 3 sets in groups with
260 20-s and 60-s rest periods, while in the group with a 180-s rest period, change in muscle
261 thickness was observed only after completing 12 sets of RE. To the best of our knowledge, this
262 is the first study to indicate that low-loaded RE with shorter rest period can generate effects on
263 muscle swelling even after low-repetition RE, which is consistent with the hypothesis of our
264 study. However, no difference was found between the three groups in percent changes in muscle
265 thickness, which is inconsistent with the hypothesis of our study.

266 A previous study ¹³ demonstrated that even at the low-load of 30% 1RM, RE for knee
267 extension consisting of 3 sets with 10 repetitions (3 s concentric, 1 s isometric, and 3 s eccentric
268 contractions) and a 60-s rest between sets for 12 weeks in healthy older adults could induce
269 muscle hypertrophy. In addition, our previous study ⁷ also indicated that even with the low-
270 load of 30% 1RM, 12sets of low-loaded resistance training could generate effects on muscle
271 hypertrophy similar to those of high-load resistance training after 8-week resistance training.
272 Based on these findings, RE consisting of 12 sets with 10 repetitions (3 s concentric, 1 s

273 isometric and 3 s eccentric contraction) was selected in the present study as a protocol that
274 could cause future muscle hypertrophy. Muscle swelling immediately after exercise is a
275 response to metabolic stress to skeletal muscle.^{26,40} Several studies have reported that muscle
276 swelling results in an increase in protein synthesis and leads to reinforcement of the
277 ultrastructure.^{28,41,42} Because the increase in muscle thickness, i.e. muscle swelling was
278 observed after RE, it is possible that the training protocols in this study might be enough
279 stimulation to induce muscle hypertrophy after chronic RE routine.

280 In this study, increases in muscle thickness were observed after 3 sets in the 20-s and
281 60-s groups. However, the increase in muscle thickness in the 180-s group was only observed
282 after 12 sets of RE. The increase in muscle thickness immediately after exercise may be due to
283 alterations in intra- and extracellular water balance induced by increased vascular
284 permeability,²⁷ which may accelerate water uptake in muscle cells according to permeability.³⁰⁻
285 ³² Concerning the rest period between sets, Villanueva, et al.²⁰ reported that resistance training
286 with a shorter rest period caused greater acute effects of hormone secretion than a longer rest
287 period. The greater increase in muscle thickness in our study may also be explained by the
288 influence of the release of metabolites at an earlier stage of RE due to shorter rest periods, even
289 when lower-repetition exercise is performed. As for the percent change in muscle thickness, no
290 significant difference was found among the three groups after 3, 6, 9 and 12 sets of RE.
291 However, the time-course in muscle thickness showed that exercise with 20-s and 60-s rest

292 periods can induce muscle swelling after as few as 3 sets. These results suggest that exercise
293 with shorter rest periods could possibility induce greater metabolic stress.

294 Over the time-course in muscle activity during exercise, the most significant change
295 in muscle activity was evident at 10–12 sets in the two groups with shorter rest periods, i.e., the
296 20-s and 60-s groups. Previous studies reported that RE with a shorter rest period between sets
297 could induce greater muscle fatigue than with a longer rest period⁴³ and that higher numbers of
298 training sets could promote greater muscle activity.⁴⁴ Therefore, in this study, we suggest that
299 performing RE with shorter rest period can increase fiber recruitment to sustain a constant
300 torque, which might lead to greater muscle activity.

301 This study has several limitations. First, we investigated only acute effects on muscle
302 thickness immediately after RE. Further studies are required to clarify differences in the effects
303 of long-term intervention of RE on muscle strength and muscle hypertrophy in relation with
304 rest periods between sets. Another limitation of this study was that it included only healthy
305 men. Although low-loaded resistance training is often prescribed for older adults or patients
306 who cannot perform high-loaded resistance training, it is not yet clear whether low-loaded
307 training in these groups can have the same acute effects as in young adults. Further studies
308 including older adults or patients with muscle weakness are needed to address these questions.

309 This study investigated the acute effects of the low-loaded, high-repetition RE with
310 varying between-set rest periods on muscle swelling. Our results showed that muscle thickness

311 significantly increased after 3 sets in the 20-s and 60-s groups, nevertheless the percent changes
312 in muscle thickness were not different among three groups. Our findings suggest that low-
313 loaded RE with shorter rest periods could cause exercise-induced muscle swelling even after
314 low-repetition RE.

315

316

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320

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322

CONFLICT of INTERESTS

323 The authors declare that there is no conflict of interests regarding the publication of this
324 article.

325

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463

464 **Figure Legends**

465 Figure 1. Muscle activity averaged over every 3 sets during RE

466 The values are shown as mean \pm standard deviation

467 20 s = 20 seconds of rest period between sets; 60 s = 60 seconds of rest period between sets;

468 180 s = 180 seconds of rest period between sets

469 * $p < 0.05$: significantly different between sets

470 # $p < 0.1$: different between sets

471

Table 1. Characteristics and training loads

	All subjects	Rest period		
		20 s (n=14)	60 s (n=14)	180 s (n=14)
Age (years)	22.9 ± 2.4	22.9 ± 2.5	22.8 ± 2.7	22.9 ± 2.1
Height (cm)	172.1 ± 5.4	170.7 ± 4.8	172.3 ± 5.6	173.3 ± 5.8
Body mass (kg)	65.6 ± 6.5	64.4 ± 6.4	65.3 ± 6.7	67.0 ± 6.5
1 repetition maximum (Nm)	100.0 ± 17.9	100.0 ± 17.5	100.0 ± 18.4	100.0 ± 19.2
Weights during resistance exercise (kg)	8.6 ± 1.4	8.7 ± 1.3	8.6 ± 1.4	8.5 ± 1.6

Values are expressed as mean ± standard deviation

20 s = 20 seconds of rest period between sets; 60 s = 60 seconds of rest period between sets; 180 s = 180 seconds of rest period between sets

Table 2. Changes in muscle thickness immediately after resistance exercise (mm)

	Pre	3 sets	6 sets	9 sets	12 sets
20 s	23.2 ± 0.7	24.1 ± 0.7*	24.1 ± 0.6*	24.4 ± 0.7*	24.3 ± 0.7#
Percent change from Pre (%)		3.9 ± 3.3	4.3 ± 2.7	5.3 ± 5.0	4.9 ± 5.9
(ES)		(0.881)	(0.847)	(0.797)	(0.663)
60 s	23.7 ± 0.8	25 ± 0.8*	25.1 ± 0.9*	25.3 ± 0.9*	25.3 ± 0.8*
Percent change from Pre (%)		5.9 ± 3.8	6.0 ± 2.8	6.7 ± 4.3	6.8 ± 1.7
(ES)		(0.881)	(0.864)	(0.864)	(0.881)
180 s	23.5 ± 1.4	24.2 ± 1.4	24.3 ± 1.5#	24.1 ± 1.5	24.5 ± 1.4*
Percent change from Pre (%)		3.0 ± 4.2	3.5 ± 5.3	2.7 ± 4.2	4.3 ± 3.1
(ES)		(0.596)	(0.663)	(0.562)	(0.814)

Values are expressed as mean ± standard deviation

20 s = 20 seconds of rest period between sets; 60 s = 60 seconds of rest period between sets; 180 s = 180 seconds of rest period between sets

Pre = before exercise; 3 sets = after 3 sets of exercise; 6 sets = after 6 sets of exercise; 9 sets = after 9 sets of exercise. 12 sets = after 12 sets of exercise

ES = effect size between Pre and each sets.

*p < 0.05: compared with pre

#p < 0.1: compared with pre

