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ACE Genotype and the Muscle Hypertrophic and Strength Responses to Strength Training

DAVID E. CHARBONNEAU¹, ERIK D. HANSON¹, ANDREW T. LUDLOW¹, MATTHEW J. DELMONICO^{1,2}, BEN F. HURLEY¹, and STEPHEN M. ROTH¹

¹ Department of Kinesiology, School of Public Health, University of Maryland, College Park, MD

² Department of Kinesiology, University of Rhode Island, College of Human Science and Services, Kingston, RI

Abstract

Purpose—Previous studies have linked an insertion/deletion polymorphism in the angiotensin-converting enzyme (*ACE*) gene with variability in muscle strength responses to strength training (ST), though conclusions have been inconsistent across investigations. Moreover, most previous studies have not investigated the influence of sex on the association of *ACE*I/D genotype with muscle phenotypes. The purpose of this study was to investigate the association of *ACE* genotype with muscle phenotypes before and after ST in older men and women.

Methods—Eighty-six inactive men and 139 inactive women, ages 50–85 yr (mean: 62 yr), were studied before and after 10 wk of unilateral knee extensor ST. The one-repetition maximum (1RM) test was used to assess knee extensor muscle strength, and computed tomography was used to measure quadriceps muscle volume (MV). Differences were compared among *ACE* genotype groups (II vs ID vs DD).

Results—Across the entire cohort at baseline, *ACE* genotype was significantly associated with total lean mass and body weight, with higher values in DD genotype carriers (both $P < 0.05$). At baseline, DD genotype carriers exhibited significantly greater MV compared with II genotype carriers for both the trained leg (men: 1828 ± 44 vs 1629 ± 70 ; women: 1299 ± 34 vs 1233 ± 49 ; $P = 0.02$) and untrained leg (men: 1801 ± 46 vs 1559 ± 72 ; women: 1268 ± 36 vs 1189 ± 51 ; $P = 0.01$), with no significant genotype \times sex interaction. No *ACE* genotype associations were observed for the 1RM or MV adaptations to ST in either men or women.

Conclusions—In the present study, *ACE* genotype was associated with baseline differences in muscle volume, but it was not associated with the muscle hypertrophic response to ST.

Keywords

ANGIOTENSIN-CONVERTING ENZYME; GENETICS; MUSCLE MASS; MUSCLE SIZE; SKELETAL MUSCLE

Muscle strength and mass are heritable phenotypes, with a heritability range of 14–80% for strength (1,21,28,30) and 20–85% for muscle mass (1,14,24,28). Although the heritability of the adaptation of these muscle phenotypes to strength training (ST) has not been well studied, the adaptive response also appears to have a genetic component (26,27).

Few specific candidate genes have been identified as being important to the response of muscle phenotypes to ST (20). One gene that has emerged as a candidate is angiotensin-converting enzyme (*ACE*), which converts angiotensin I to angiotensin II. An insertion/deletion (I/D) polymorphism in this gene has been found to be responsible for half of the variation in *ACE* enzyme activity (22,36), with those who carry the deletion (D) allele having higher *ACE* enzyme activity (6). Homozygotes for the I allele (II) have significantly less *ACE* activity than heterozygotes (ID), and heterozygotes have lower *ACE* activity than homozygotes for the D allele (DD) (31,35).

Angiotensin II has been linked to overload-induced cardiac hypertrophy (18,23,25) and smooth-muscle hypertrophy (4,8). *ACE* inhibitors have been shown to inhibit hypertrophy in overloaded muscles (10,34), suggesting a role for angiotensin II in skeletal muscle hypertrophy. McBride (16) found that blocking angiotensin II's AT1 receptor attenuated eccentric training-induced hypertrophy and strength gains in Sprague–Dawley rats, providing additional evidence for the role of the renin–angiotensin system (RAS), and *ACE* in particular, in overload-induced muscle hypertrophy.

Studies investigating the association of *ACE* genotype with skeletal muscle strength and mass phenotypes have yielded inconsistent results. Williams et al. (35) report a positive association between the D allele and baseline muscle strength. Folland et al. (7) and Giaccaglia et al. (9) both show a gene \times ST interaction, such that carriers of the D allele (DD + ID) had greater ST-induced increases in strength compared with the II genotype. In contrast, Williams et al. (35) fail to show an association between *ACE* genotype and the response of muscle strength to ST. Similarly, Pescatello et al. (19) and Thomis et al. (29) fail to support the relationship between the D allele and muscle strength adaptation to ST. The few studies that have investigated the association between *ACE* genotype and muscle size responses to ST have observed no association in muscles of the upper arm (19,29), but no studies have examined the association in the weight-bearing lower limbs.

The purpose of the present study was to investigate the association of *ACE* genotype with muscle phenotypes before and after ST in older men and women. Though the literature is inconclusive, the biological rationale suggests an advantage for the D allele with regard to muscle phenotypes; thus, we hypothesized that the D allele would be associated with higher values for muscle phenotypes before ST, and greater increases in muscle phenotypes in response to ST. As most studies have investigated only men, we investigated men and women to determine possible sex differences.

METHODS

Subjects

Participants in the study consisted of 243 inactive, healthy volunteers between the ages of 50 and 85 yr. For this investigation, “inactive” was operationally defined as a person who performs less than 20 min of vigorous activity per week. Subjects were required to be nonsmokers with no significant cardiovascular, metabolic, or musculoskeletal conditions that could limit their ability to perform heavy resistance exercise. Subjects who were already taking medications for more than 3 wk were included in the study, with the understanding that they would maintain the same medicine and dosage for the entirety of the study. Medication use was classified into four categories for their potential influence on muscle phenotypes: diuretics, *ACE* inhibitors, hormone therapy, and antiinflammatory/pain reducers. After all methods and procedures were explained, volunteers who chose to participate were required to read and sign a written consent form that was approved by the institutional review board of the University of Maryland, College Park. Throughout the study, subjects were continually reminded not to alter their physical

activity levels or habitual dietary intake, and body weight was measured weekly to confirm the absence of weight loss or gain.

Body composition

Body composition was analyzed using dual-energy x-ray absorptiometry (DXA), using fan-beam technology (model QDR 4500A, Hologic, Waltham, MA) as previously described (11). In short, a standardized procedure for subject positioning and use of the QDR software was used to perform full-body scans at baseline and again on completion of the ST intervention. The scans were analyzed for fat-free mass (FFM), fat mass, and body fat percentage. FFM included both lean soft tissue and total bone mass. The scanner was calibrated daily with calibration blocks and weekly with a whole-body phantom. The coefficients of variation (CV) for all body composition measures were calculated from repeated scans of 10 subjects who were scanned three consecutive times with repositioning. The CV was 0.6% for FFM and 1.0% for percent fat.

Strength testing

The full description of the strength testing methods that were used in this study were previously described in a report from our laboratory (11). In short, one-repetition maximum (1RM) knee extensor strength tests were performed on both legs separately prior to and at the completion of the ST intervention. These tests assessed knee extension strength and were performed on the same air-powered resistance machines (Keiser Sports/Health Equipment, Fresno, CA) that were used during the ST. These tests used objective criteria and a light system that indicated a successful attempt when the knee was extended to approximately 165°, to provide a standardized measure of knee extensor strength.

Muscle volume testing

A full description of the methods used to measure muscle volume has been reported previously (11). Briefly, quadriceps muscle volume was measured on both the trained and untrained thighs at baseline and after training using computed tomography (CT) imaging. Axial sections (10 mm thick) of each thigh were obtained every 40 mm between the most distal point of the ischial tuberosity and the most proximal boundary of the patella while the subject was placed in the supine position. Quadriceps muscle volume was estimated using a 4-cm interval between the center of each section. For each section of the thigh, cross-sectional area of the quadriceps muscle group was manually outlined using Medical Imaging Processing, Analysis, and Visualization (MIPAV) software (National Institutes of Health, Bethesda, MD). This manual outlining was done on every section, starting from the border of the proximal patella and ending when the quadriceps were no longer distinguishable from the hip flexor and adductor muscle groups. Repeated-measures CV was measured for each investigator based on repeated measures of selected axial sections of one subject on separate days. Average intrainvestigator CV was 1.7% and 2.3% for the investigators, respectively. The average interinvestigator CV was 3.8%. Final muscle volume was calculated using the truncated cone formula reported by Tracy et al. (33).

ST intervention

A complete description of the ST intervention has been previously reported (11). Briefly, the ST intervention consisted of approximately 10 wk of unilateral (one-legged) knee extensor training of the dominant leg, while the untrained leg served as an internal control. During the 10-wk period, subjects performed the training protocol three times per week (1–2 d separating training sessions), with each training session lasting approximately 30 min. The training protocol included multiple sets of unilateral knee extension exercise designed to individualize loads in a way that elicited near-maximal effort on all exercise repetitions while maintaining

a high training volume. Subjects continued to ST until all after-training measurements were completed; at minimum, 24 h separated any post-ST measurements from a training session.

Genotyping

DNA was extracted from whole-blood samples using standard procedures (Gentra PureGene System, Minneapolis, MN). The *ACE* I/D polymorphism was genotyped using a polymerase chain reaction (PCR)-based DNA amplification, using flanking primers. The sense primer sequence was 5' CTGGAGACCACTCCCATCCTTTTCT 3', and the antisense primer was 5' GATGTGGCCATCACATTCGTCAGAT 3' (31). Genotyping was performed by separating the PCR amplicon on a 2% agarose gel with ethidium bromide staining. Positive control samples for each genotype were obtained through direct DNA sequencing and were used to validate all genotyping assays.

Statistical analysis

Statistical analyses were performed using SPSS version 13.0 for Mac OS X (Chicago, IL). Chi-square analysis was used to test for Hardy–Weinberg equilibrium. Analysis of covariance (ANCOVA) was used to compare baseline values among *ACE* genotype groups, with repeated-measures ANCOVA used to compare ST adaptations; LSD *post hoc* analyses were used to test specific contrasts when necessary. Analyses were performed, both across all genotype groups and between D-allele carriers and noncarriers (DD + ID genotypes vs II genotype). D-allele carriers were combined on the basis of the biological rationale surrounding the D-allele, as well as to allow comparison with other studies that performed similar analyses. Covariates included age, height (or BMI), and race, with sex included as an independent variable. Medication use was tested as a potential covariate but was not found to be significant in any of our analyses. Because there were significant differences between men and women for the muscle phenotypes of interest, analyses were also stratified by sex. Baseline characteristics are presented as means with standard deviations. All other data are presented as least squared means \pm standard error. Statistical significance for all analyses was accepted at $P = 0.05$.

Sample size estimates were calculated *a priori* on the basis of an alpha of 0.05, phenotype differences between genotype groups of 15–25% (depending on the variable of interest), and statistical power of 80%. Using this information and the within-subject standard deviation from our previous data in healthy adults between the ages of 50 and 74 yr (13,32), our minimal estimated sample size ranged from 64 to 67 subjects per genotype group at baseline and from 56 to 57 subjects per genotype group after ST (depending on the variable of interest). When accounting for unbalanced samples sizes using harmonic means, we approximated this level of statistical power for the overall study (harmonic mean sample size of 64 per group at baseline and 50 per group after ST). We were underpowered for sex-specific comparisons where sample sizes are lower, so those analyses should be considered exploratory.

RESULTS

Subject characteristics

Characteristics of participants by *ACE* genotype and sex are shown in Table 1. Table 2 shows the genotype and allele frequencies for all subjects separated by race (147 whites, 81 blacks). Although genotype frequencies deviated from Hardy–Weinberg equilibrium in whites ($P < 0.05$), repeat genotyping with positive control samples confirmed genotype accuracy. Significant differences were observed for weight and FFM among *ACE* genotype groups (both $P = 0.04$); these results were driven by differences among males, with DD genotype carriers exhibiting greater weight (91.6 ± 1.8 ; $P = 0.04$) and FFM (62.6 ± 1.0 kg; $P = 0.01$) compared with II homozygotes (weight: 82.1 ± 3.3 kg; FFM: 57.1 ± 1.9 kg) when covaried for age, height, and race.

Baseline muscle strength and volume

Baseline values for 1RM and quadriceps MV are shown in Table 3. No significant genotype differences were observed for 1RM at baseline across the entire cohort for either the trained or untrained leg. Significant genotype differences were observed for baseline MV (age, race, and height as covariates) in both the trained and untrained leg across the entire cohort (both $P \leq 0.02$; Table 3). These differences remained if BMI was used in place of height as a covariate. Genotype \times sex interactions were not significant ($P = 0.25\text{--}0.38$), indicating higher baseline MV values in both male and female DD genotype carriers compared with II genotype carriers.

Muscle adaptation to ST

The 1RM and quadriceps MV adaptations to ST are shown separately by sex in Tables 4 and 5. Both 1RM and MV improved significantly in response to ST in the trained leg across all three genotype groups (both $P < 0.01$). When using age, race, and height as covariates, no genotype differences were observed in either the trained or untrained leg for either 1RM or MV. Similar findings were observed when BMI replaced height as a covariate, or when MV was used as a covariate for the 1RM analysis. No significant genotype \times sex interactions were observed. Analysis of D-allele carriers (DD + ID) vs II carriers also yielded no significant differences (Tables 4 and 5).

DISCUSSION

The results of the present study provide evidence of an association of the *ACE* I/D genotype with baseline quadriceps muscle volume in both men and women, but no evidence of association with the response of either knee extensor 1RM or quadriceps muscle volume to ST. The present study extends previous, inconclusive findings by examining one of the largest cohorts studied to date, including both men and women. When viewed in total, the findings of the present and previous investigations indicate the possibility that *ACE* I/D genotype plays a minor role in muscle development, though importance for muscle adaptation to ST appears limited.

Our finding of no association between *ACE* genotype and baseline strength supports earlier findings by Folland et al. (7), Kritchevsky et al. (12), and Pescatello et al. (19), who conclude that *ACE* genotype was not associated with muscle strength in either the upper arm (19) or the leg (7,12). In contrast, Williams et al. (35) report a significant association between *ACE* genotype and pretraining isometric and isokinetic strength in the knee extensors, with DD homozygotes having the highest strength levels (35). Williams and colleagues (35) suggest that Folland et al. (7) would have seen an association at baseline if their study had greater statistical power, though that issue is not likely for the large studies by Kritchevsky et al. (12) and Pescatello et al. (19). With regard to training adaptations, Folland et al. (7) found that the isometric and isokinetic strength response to isometric ST was associated with *ACE* genotype and that the D-allele carriers experienced significantly greater strength increases than II homozygotes, though training specificity issues make interpretation of these data difficult. More recently, Giaccaglia et al. (9) have reported similar results in a population of obese older adults, such that 18 months of walking and light weight training resulted in greater gains in knee extensor strength in DD homozygotes compared with II homozygotes (9). In contrast, Pescatello et al. (19) report greater increases in maximal voluntary contraction with training in carriers of the I allele than in DD homozygotes, and Thomis and colleagues (29) show no association with muscle adaptation to ST. Thus, previous studies present conflicting results regarding the potential role for *ACE* genotype with muscle strength phenotypes.

In the present study, we observed higher muscle volume in DD genotype carriers at baseline for both men and women, but no associations with the muscle volume adaptation to ST.

Previous studies that have investigated the association of *ACE* genotype with the muscle size response to ST have observed no association (19,29). Those investigations differed from the present study in that they examined cross-sectional area of the muscles of the upper arm, while the present study examined muscle volume of the quadriceps. Whether the weight-bearing nature of the lower limbs compared with the upper limbs is relevant is open to speculation. In general, however, the available data regarding *ACE* genotype and skeletal muscle indicate that any influence is minor and of little clinical significance, independent of the many other genes likely to be contributing to these phenotypes.

Although not addressed in the present study, a possible mechanism through which *ACE* genotype could influence skeletal muscle size is through the production of angiotensin II. The *ACE* enzyme acts as a growth factor in cardiac (17,23) and smooth muscle cells (4,8), and Montgomery et al. (18) show greater left ventricular hypertrophy in response to exercise in D-allele carriers compared with II homozygotes. Decreased levels of angiotensin II, resulting from *ACE* inhibition, have also been shown to attenuate overload-induced skeletal muscle hypertrophy in animal models (10,34). Similarly, blocking the AT₁ receptors through which angiotensin II signals muscle cells can attenuate exercise-induced skeletal muscle hypertrophy (16). In the animal studies, *ACE* inhibition was used to decrease the production of angiotensin II, which is similar to human II homozygotes for the *ACE* gene, whose conversion of angiotensin I to angiotensin II is lower than D-allele carriers (5). Whether this mechanism results in the genotype differences in baseline MV (e.g., muscle development) seen in the present study is uncertain, though *ACE* would be one of many contributing genes if this mechanism were confirmed.

Determining the genotypes that contribute to skeletal muscle phenotypes may someday be important for identifying people who are, for example, predisposed to sarcopenia or who may be predicted as nonresponsive to a ST program. Such work is in its infancy, but that rationale underlies the concept of genomic or personalized medicine. The work presented here is another example of efforts to identify the most important candidate genes for specific phenotypes, which may someday have clinical importance for personalized prevention and treatment efforts. Ultimately, many interacting genes will contribute to health-related phenotypes, but identifying those with the greatest influence will help speed potential clinical relevance. On the basis of the data presented here, and that of other studies in the literature, *ACE* does not seem to be a gene with strong clinical relevance for skeletal muscle phenotypes, though the potential exists that important interactions between *ACE* and other genes may be identified in future studies.

ACE genotype frequencies have been shown to differ among race groups (2,3,15). Commonly, the allele frequency among individuals of European descent (whites) for this I/D polymorphism is approximately 50% for both the I and D alleles compared with 41% and 59% for the I and D alleles, respectively, in individuals of African descent (blacks) (15). In the present study, the frequency of the D allele among whites was abnormally high (65%), driving the genotype frequencies out of Hardy–Weinberg equilibrium. We are uncertain why our subject pool had this abnormal allele frequency. Our genotyping protocol was a commonly accepted and used protocol (31) that was validated using direct DNA sequencing. Thus, our sample distribution appears skewed by random chance. The suburban Washington, DC, area from which these subjects were recruited is remarkably diverse, which reduces the possibility that our recruitment targeted isolated populations. Our sample sizes for the overall study were balanced across all three genotype groups, which should minimize the chance of a spurious statistical result.

As with gene association studies in general, the need for replication of the present data in an independent cohort could be argued, though, as stated above, the fact that very little consistency

has been observed in the literature to date argues against *ACE* as a major contributing gene for skeletal muscle traits. In effect, the present study represents a type of replication of the previous studies described above, in that this study investigated the same associations between *ACE* genotype and muscle phenotypes before and after an ST intervention, though differences in methodology prevent clear comparisons. Consideration of the findings of this study along with those in the previously existing literature leads us to conclude that *ACE* genotype appears to have at best a minor influence on muscle size in the lower limb, though mechanistic details are unclear.

In summary, the results of the present study, in combination with previous studies examining *ACE* genotype and skeletal muscle, indicate that the *ACE* I/D genotype is not a major determinant of skeletal muscle strength or size or their response to ST, but it may play a minor role in baseline muscle size. Differences in muscle strength and mass variables, as well as differences in the muscle groups targeted for study, make comparisons across studies challenging, which may account for some of the inconsistency in the literature. We conclude, however, that if *ACE* genotype were a major contributor to skeletal muscle phenotypes (independent of other genes), then some consistency would be apparent in the literature even despite these study design differences, and such consistency is notably absent.

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TABLE 1

Subject characteristics by sex and ACE genotype.

	Men				Women			
	II	ID	DD	DD	II	ID	DD	DD
Baseline study population	14	26	46	68	28	43	68	68
After-ST study population	13	24	35	44	21	27	44	44
Age (yr)	62.8 (8.5)	63.8 (7.6)	62.2 (8.8)	61.5 (9.5)	64.7 (9.0)	61.8 (8.6)	61.5 (9.5)	61.5 (9.5)
Height (cm)	173.5 (5.7)	173.9 (6.9)	175.8 (7.7)	162.7 (6.0)	162.1 (6.4)	163.1 (5.8)	162.7 (6.0)	162.7 (6.0)
Weight (kg)	80.8 (10.4)	87.7 (11.0)	92.7 (15.4)*	75.7 (15.8)	73.4 (15.1)	77.8 (15.0)	75.7 (15.8)	75.7 (15.8)
After-ST weight	81.4 (11.5)	88.1 (11.1)	90.2 (14.8)	75.2 (20.1)	73.4 (15.1)	75.4 (16.1)	75.2 (20.1)	75.2 (20.1)
BMI (kg·m ⁻²)	26.8 (2.6)	28.9 (3.6)	29.9 (4.6)	28.9 (5.7)	27.9 (5.6)	29.3 (5.5)	28.9 (5.7)	28.9 (5.7)
After-ST BMI	27.0 (3.0)	29.2 (3.6)	29.1 (4.3)	28.2 (7.4)	27.9 (6.1)	28.6 (6.0)	28.2 (7.4)	28.2 (7.4)
FM (kg)	22.0 (5.0)	25.2 (6.5)	26.3 (8.1)	30.9 (10.0)	29.8 (10.1)	31.7 (9.3)	30.9 (10.0)	30.9 (10.0)
After-ST FM	22.4 (6.1)	24.9 (6.4)	25.1 (7.4)	30.8 (10.8)	28.8 (10.7)	29.2 (10.0)	30.8 (10.8)	30.8 (10.8)
FFM (kg)	56.2 (6.8)	59.8 (6.5)	63.2 (9.0)*	43.6 (6.5)	41.5 (5.9)	44.0 (6.8)	43.6 (6.5)	43.6 (6.5)
After-ST FFM	56.4 (6.7)	60.5 (6.2)	62.3 (8.5)	43.7 (6.9)	42.5 (5.2)	43.2 (6.6)	43.7 (6.9)	43.7 (6.9)

Data are means (SD). N, number of subjects; FM, fat mass; FFM, fat-free mass; ST, strength training.

* Body weight and FFM were significantly greater in DD vs II homozygotes in men, as discussed in the Results section.

TABLE 2

ACE I/D genotype and allele sample sizes and frequencies by race.

	II	ID	DD	I Allele	D Allele
Total (%)	42 (18.7%)	69 (30.7%)	114 (50.7%)	34.0%	66.0%
Whites (%)	30 (20.5%)	43 (29.5%)	73 (50.0%)	35.3%	64.7%
Blacks (%)	12 (15.2%)	26 (32.9%)	41 (51.9%)	31.6%	68.4%

TABLE 3

Baseline muscle strength and mass values by sex and ACE genotype.

	Men			Women		
	II	ID	DD	II	ID	DD
<i>N</i>	14	26	46	28	43	68
IRM for trained leg	31.8 ± 1.4	31.1 ± 1.1	33.8 ± 0.9	19.6 ± 1.0	20.1 ± 0.9	20.1 ± 0.7
IRM for untrained leg	30.8 ± 1.5	29.4 ± 1.2	32.2 ± 1.0	18.8 ± 1.1	18.8 ± 1.0	18.8 ± 0.8
MV for trained leg	1629 ± 70	1759 ± 52	1828 ± 44*	1233 ± 49	1255 ± 41	1299 ± 34*
MV for untrained leg	1559 ± 72	1728 ± 54	1801 ± 46*	1189 ± 51	1214 ± 42	1268 ± 36*

Data are least squared means ± standard error. *N*, number of subjects; MV, muscle volume.

* Significant differences were observed for MV between DD and II genotype groups for both the trained ($P = 0.02$) and untrained ($P = 0.006$) legs in both men and women (genotype × sex interactions $P = 0.25-0.38$).

TABLE 4

Muscle strength and mass adaptations to strength training by ACE genotype for men.

	II	ID	DD	II	DD+ID
	13	24	35	13	59
Trained leg					
Baseline IRM (kg)	33.1 ± 1.5	30.6 ± 1.1	33.3 ± 1.0	33.1 ± 1.5	32.1 ± 0.8
After-ST IRM (kg)	40.1 ± 1.6	39.4 ± 1.2	41.3 ± 1.1	40.1 ± 1.6	40.5 ± 0.9
Δ IRM (kg)	5.1 ± 1.0	6.4 ± 0.7	5.8 ± 0.7	5.1 ± 1.0	6.5 ± 0.3
Baseline MV (cm ³)	1676 ± 66	1737 ± 51	1817 ± 45	1676 ± 66	1783 ± 36
After-ST MV (cm ³)	1848 ± 72	1907 ± 55	1985 ± 49	1848 ± 72	1952 ± 40
Δ MV (cm ³)	176.1 ± 22.2	167.4 ± 16.7	169.7 ± 13.5	176.1 ± 22.2	169.1 ± 10.2
Untrained leg					
Baseline IRM (kg)	32.0 ± 1.6	28.4 ± 1.2	31.2 ± 1.1	32.0 ± 1.6	30.0 ± 0.9
After-ST IRM (kg)	33.1 ± 1.7	32.5 ± 1.3	34.1 ± 1.2	33.1 ± 1.7	33.4 ± 1.0
Δ IRM (kg)	1.0 ± 1.0	3.0 ± 0.8	2.2 ± 0.7	1.0 ± 1.0	2.6 ± 0.3
Baseline MV (cm ³)	1604 ± 68	1703 ± 53	1791 ± 47	1604 ± 68	1753 ± 38
After-ST MV (cm ³)	1628 ± 70	1706 ± 54	1777 ± 48	1628 ± 70	1747 ± 39
Δ MV (cm ³)	25.5 ± 17.1	2.9 ± 12.9	-11.5 ± 10.4	25.5 ± 17.1	-6.6 ± 8.0

Data presented as least squared means ± SE. Sample sizes (N) represent the number of subjects who completed the ST protocol. The increases in both IRM and MV with ST in the trained leg (baseline vs post-ST values) were statistically significant in all groups ($P < 0.05$). No significant genotype differences were observed.

TABLE 5

Muscle strength and mass adaptations to strength training by ACE genotype for women.

N	II	ID	DD	II	DD + ID
	21	27	44	21	71
Trained leg					
Baseline IRM (kg)	19.8 ± 1.2	19.2 ± 1.1	19.5 ± 0.8	19.8 ± 1.2	19.4 ± 0.7
After-ST IRM (kg)	25.1 ± 1.3	24.7 ± 1.2	24.6 ± 0.9	25.1 ± 1.3	24.7 ± 0.8
Δ IRM (kg)	3.9 ± 0.8	4.0 ± 0.7	3.8 ± 0.6	3.9 ± 0.8	6.5 ± 0.6
Baseline MV (cm ³)	1225 ± 53	1260 ± 47	1257 ± 38	1225 ± 53	1260 ± 31
After-ST MV (cm ³)	1324 ± 57	1346 ± 52	1361 ± 41	1324 ± 57	1357 ± 34
Δ MV (cm ³)	99.1 ± 10.2	84.2 ± 9.2	104.3 ± 7.2	99.1 ± 10.2	97.4 ± 8.7
Untrained leg					
Baseline IRM (kg)	19.4 ± 1.3	18.4 ± 1.1	18.9 ± 0.9	19.4 ± 1.3	18.8 ± 0.8
After-ST IRM (kg)	21.3 ± 1.4	20.8 ± 1.3	20.3 ± 1.0	21.3 ± 1.4	20.5 ± 0.9
Δ IRM (kg)	1.5 ± 0.8	1.9 ± 0.8	1.1 ± 0.6	1.5 ± 0.8	1.4 ± 0.5
Baseline MV (cm ³)	1193 ± 54	1253 ± 49	1233 ± 39	1193 ± 54	1242 ± 35
After-ST MV (cm ³)	1205 ± 56	1257 ± 51	1240 ± 41	1205 ± 56	1248 ± 33
Δ MV (cm ³)	12.3 ± 8.6	2.5 ± 7.7	5.5 ± 6.1	12.3 ± 8.6	5.4 ± 6.9

Data presented as least squared means ± SE. Sample sizes (N) represent the number of subjects who completed the ST protocol. The increases in both IRM and MV with ST in the trained leg (baseline vs post-ST values) were statistically significant in all groups ($P < 0.05$). No significant genotype differences were observed.