Changes in Muscle Volume, Strength, and Bioenergetics during Recombinant Human Growth Hormone (GH) Therapy in Adults with GH Deficiency*

Y. J. H. JANSSEN, J. DOORNBOS, AND F. ROELFSEMA

Departments of Endocrinology (Y.J., F.R.) and Radiology (J.D.), Leiden University Medical Center, Leiden, The Netherlands

ABSTRACT
Adults with GH deficiency (GHD) suffer from muscle weakness, which can be caused by the frequently reported decrease in muscle mass. However, measurements of both muscle strength and mass of muscle tested are scarce in adults with GHD. The aim of the present study was, therefore, to investigate intrinsic muscle strength (strength expressed per muscle volume unit) in adults with GHD at baseline and after 52 weeks of recombinant human GH (rhGH) therapy given in low, more physiological doses. A second objective was to investigate the influence of GH on muscle bioenergetics in the resting muscle. Isometric and isokinetic quadriiceps strengths were measured in 28 males with GHD and in healthy controls matched for age and height. Quadriiceps mass, determined by magnetic resonance imaging, and muscle bioenergetics, determined by phosphorus nuclear magnetic resonance spectroscopy, were measured in 20 of 28 patients with GHD and in controls matched for age and height. All patients were treated with doses of rhGH ranging from 0.6–1.8 IU/day, given for 52 weeks. Measurements of muscle mass, strength, and bioenergetics were repeated after 52 weeks of treatment with rhGH. The mean GH dose at 52 weeks of rhGH treatment was 1.3 ± 0.8 IU/day. The mean serum insulin-like growth factor I level at baseline was 9.4 ± 0.7 nmol/L and significantly increased to 26.4 ± 1.2 nmol/L after 52 weeks of rhGH treatment. Adults with GHD had significantly reduced quadriiceps muscle mass (P = 0.034) and reduced isometric muscle strength (P = 0.002) and tended to have low isokinetic muscle strength (P = 0.06), which all improved after rhGH therapy. Intrinsic muscle strength was not significantly different in adults with GHD compared with that in healthy controls and did not change during rhGH therapy. No bioenergetic abnormalities at baseline or after rhGH therapy were found in males with GHD. In conclusion, quadriiceps muscle mass is decreased in adults with GHD and increased with rhGH therapy. These changes in muscle mass account for the changes in muscle strength found in these patients, as no changes in intrinsic muscle strength were found. (J Clin Endocrinol Metab 84: 279–284, 1999)

SINCE the introduction of recombinant human GH (rhGH), several clinical trials have examined the characteristics of GH deficiency (GHD) and the effect of GH replacement therapy in adults with GHD. Adults with GHD appear to have muscle weakness that can be improved with rhGH therapy (1–7). A main cause of the decrease in muscle strength is a decrease in muscle mass, which is frequently reported in adults with GH deficiency. Normal quadriiceps strength per thigh muscle mass, estimated by anthropometry, was reported in a small group (n = 6) of patients with childhood-onset GHD (7). However, only Cuneo et al. (1, 2) measured both muscle strength and mass of the tested muscle in adults with GHD. In their study, measurement of muscle mass was based on single slice computed tomography (CT). They have reported decreased intrinsic (isometric) strength (strength expressed per muscle unit) in 24 adults with GHD, but this did not improve after 6 months of rhGH therapy (1, 2).

The dose of rhGH used by Cuneo et al. (0.07 IU/kg/day), which was also used by others at that time, was based on doses used in children (2). Generally, this dose regimen resulted in a high incidence of side-effects, mainly related to fluid retention, and supranormal levels of serum insulin-like growth factor I (IGF-I). Half of this dose was therefore used in subsequent studies, and recently even lower (and also individualized) doses were advised (8, 9).

Muscle function is crucially dependent on the maintenance of cellular ATP homeostasis. Relative concentrations of both phosphate metabolites, such as inorganic phosphate (Pi), ATP, and phosphocreatine (PCr), and intracellular pH can be measured with the noninvasive phosphorus nuclear magnetic resonance (31P-MRS) spectroscopy. This technique is therefore useful in the study of muscle bioenergetics and hence has been used in the evaluation of metabolic disorders of muscle that present clinically with exercise intolerance (10, 11). 31P-MRS might also detect bioenergetic abnormalities or changes during rhGH therapy in adults with GHD.

The objective of this trial was to compare quadriiceps strength, quadriiceps volume and the muscle bioenergetics in a relatively large group of males with GHD and in healthy control males, pairwise matched for height and age. In addition to maximal isometric muscle strength testing, which is tested most frequently, maximal isokinetic muscle strength was tested, because the latter muscle contraction is more representative of daily living and sporting activities. Magnetic resonance imaging (MRI), which has higher sensitivity in discriminating tissues or individual muscles than CT scan-
ning, was used in the present study (12). Moreover, we have scanned multiple slices (from hip to knee). Furthermore, the effects of lower, more physiological doses of rhGH (0.6–1.8 IU/day) given for 52 weeks on muscle strength, muscle volume, and muscle energy store were studied.

**Subjects and Methods**

**Subjects**

Thirty male adults with GHD, as evidenced by a peak serum GH response of less than 7 mU/L during insulin-induced hypoglycemia, were studied. None of the patients had a body mass index greater than 32 kg/m². Two of the patients did not participate in this part of the study, 1 due to the presence of spasticity and 1 due to knee complaints. Twenty-eight patients (age range, 22–70 yr) with childhood-onset (n = 7) or adult-onset (n = 21) GHD underwent maximal muscle strength testing. A subgroup of 20 patients also underwent MRI and 31P-MRS.

The estimated age of onset of GHD was 30 yr (range, 0–61 yr), with an estimated duration of GHD state of 18.5 yr (range, 1–56 yr). Three patients had isolated GHD, but the vast majority had additional pituitary hormone deficiencies: LH/FSH deficiency (n = 2), total anterior pituitary gland failure (n = 17), and total pituitary gland failure (anterior and posterior) (n = 6). All patients except one received substitution therapy in the form of gonadal steroids (testosterone, 250 mg, im every 3, 4, or 2 weeks (n = 3, 11, and 3, respectively); daily testosterone undecanoate, 120–160 mg, orally (n = 4 and 3); hCG, 1500 IU weekly (n = 1); fluoxymesterone, 10 mg daily (n = 1)]. T₄, hydrocortisone, and desmopresin were given as indicated.

The etiology in the patients with childhood-onset GHD was idiopathic or related to birth trauma. Three of these patients had received GH during childhood. The etiology of GHD in adult-onset GHD was pituitary adenoma in 13 patients: nonfunctioning adenoma (n = 10), ACTH-producing adenoma (n = 1), and prolactinoma (n = 2). In the other eight patients the etiology was trauma (n = 2), a tumor in the pituitary region (n = 5), and hydrocephalus (n = 1).

Twenty healthy controls, pairwise-matched for age (<8-yr difference) and height (<10-cm difference), underwent maximal muscle strength testing. In eight of them, muscle volume and phosphate spectroscopy were also performed. The comparison of muscle volume, muscle strength, and phosphate spectroscopy between GHD patients and (pairwise-matched) healthy subjects was thus based on eight pairs. Seven of these eight patients had adult-onset GHD, all had multiple pituitary deficiencies, age range was between 22–67 yr, and the range in height was between 173.3–186.0 cm. Patients with a history of Cushing’s disease were not included in this part of the study.

Informed consent was obtained from all subjects, and the study was approved by the ethics committee of the Leiden University Medical Center.

**Muscle strength**

Muscle strength in the knee extensor was measured with an EN-Knee dynamometer (DIMEQ, Delft Instruments, Delft, The Netherlands), which consists of a fixed length lever arm with a mechanically limited range of motion. Isokinetic and isometric muscle strength were measured at 120°/s and 45°, respectively. Subjects were positioned in the test chair with the lower left leg secured to the shin pad above the ankle, and hip and thigh strapped down to avoid involuntary movements. Some knee movements were made for familiarization with the procedure after verbal explanation. The isokinetic exercise protocol consisted of extending the knee 15 times in rapid succession. After 10–15 min of rest, isometric muscle strength was measured. Three brief (3 to 5 s) maximal voluntary isometric contractions alternated by 60 s of rest were performed. Isokinetic muscle strength was expressed as the maximum peak torque produced in the knee extensions. Maximal isometric strength was the highest value of three obtained. The mean coefficients of variation for isokinetic and isometric muscle testing were 4.4% and 4.3%, respectively. Verbal encouragement was given by the same person in a standardized manner.

**Muscle volume**

Cross-sectional images of the upper left leg were obtained using a 1.5-T MRI scanner (Gyrosan S15, Philips Medical Systems, Best, The Netherlands) in 20 patients with GHD and in 8 healthy controls. Contiguous T1-weighted transverse images (thickness, 10 mm; no interslice gap) were specified from the coronal scout image from the femoral to the femoral-tibial space.

Calculation of quadriceps area/volume was performed by a single observer on a SUN-SPARC workstation using an image-analyzing computer program based on a seed-growing procedure as described by Elbers et al. (13). The coefficient of variation for partial quadriceps volume (sum of 12 slices) was less than 1.5%.

Total quadriceps volume was measured in the eight healthy controls. Total quadriceps volume and the volume of different parts (distal, proximal, or middle parts) and portions (one slice to multiple slices) of the quadriceps volume were correlated with muscle strength. The muscle volume in the slice with the maximum quadriceps area and the volume at midthigh (an often used site when only one slice is scanned) were also correlated with muscle strength.

The part of the total quadriceps volume that best estimated muscle strength was used to compare baseline values with measurement during rhGH treatment and to correlate (isometric and isokinetic) strength with volume in the patients with GHD.

**31P-MRS**

All experiments were performed on a 1.5-T whole body MR system (Gyrosan S15, Philips Medical Systems) using a 10-cm diameter transmit/receive, single tuned, P-31 surface coil positioned over the midvastus lateralis of the patient. Shimming of the magnetic field was performed with the proton imaging body coil, yielding a water resonance of 0.2–0.3 parts/million full width at half-maximum. The 31P-MR spectra were obtained using a pulse repetition time of 5 s and a number of signal acquisitions of 64, resulting in an acquisition time of approximately 5 min. The signal to noise ratios of the spectra for ATP and PCr were 50 and 150, respectively.

The metabolite peaks in the spectra (PCr, Pi, αATP, βATP, and γATP) were quantified by curve fitting in the time domain, using a spectrum model function in which previous knowledge was incorporated (14). In the model function-fitting procedure, the amplitude, width, and spectral position of the metabolite signals are adjusted by an iterative approach until the difference between the experimental and the simulated spectrum is minimized. The J-coupling patterns, the relative amplitude, and the relative line widths of the three ATP resonances, however, were not allowed to vary. Thus, no constraints were used in the determination of the metabolite ratios PCr/ATP, Pi/ATP, and Pi/PCr. The relative peak amplitudes of the signals correspond to the relative concentrations of the phosphorous metabolites.

**GH therapy**

For other study objectives, patients were randomized to three groups to receive one of three dose regimens for 24 weeks (0.6, 1.2, or 1.8 IU/day; 0.2, 0.4, or 0.6 mg/day). After 24 weeks of treatment the dose of rhGH was individually adjusted, using a dose range of 0.6–1.8 IU/day, to maintain the concentration of serum IGF-I within the normal laboratory reference range. Side-effects were also taken into consideration when adjusting the dose. Treatment with rhGH was continued for 52 weeks in all patients.

**Assays**

The total serum IGF-I concentration was determined by RIA (Incstar Corp., Stillwater, MN) after extraction and purification on ODS-silica columns. The interassay coefficient of variation was less than 11%. The detection limit was 1.5 nmol/L. Age-related normal data were determined in the same laboratory. IGF-I was also expressed as a z score from age-related normal levels.

**Statistics**

Statistical analysis was performed using SPSS for Windows (SPSS, Inc., Chicago, IL; release 7.0). Results are expressed as the mean ± sem.
unless otherwise specified. Pearson’s correlation coefficient or Spearman’s correlation coefficient was used to calculate correlations. A paired *t* test was performed when adults with GHD were compared with healthy controls pairwise matched for age and height. Childhood-onset GHD patients were compared with adult-onset GHD patients by Student’s *t* test. Changes after 52 weeks of rhGH therapy were compared using a paired *t* test. Differences were considered significant for *P* < 0.05.

Results

**Patient characteristics**

The mean age of the total group of males with GHD was 48.7 ± 2.2 yr. Their mean height, weight, and body mass index were 175.5 ± 2.5 cm, 81.0 ± 3.2 kg, and 26.1 ± 3.0 kg/m², respectively. The mean serum IGF-I concentration at baseline was 9.4 ± 0.7 nmol/L (−1.8 ± 0.1 sd score).

**Quadriceps volume**

Quadriceps volume from patella to trochanter major significantly correlated with both isometric and isokinetic muscle strengths (r = 0.753 and r = 0.848, respectively; Table 1). The most significant relationship between strength and (partial) quadriceps volume, however, was found when the partial volume was based on the sum of the volume of the 12 slices (12 cm) below the lesser trochanter. Therefore, this part of the muscle was used in further analyses.

**Patients with GHD vs. healthy controls**

**Muscle volume and strength.** Patients with GHD had significantly reduced (partial) volume of the quadriceps compared to healthy subjects pairwise matched for age (<8-yr difference) and height (<10-cm difference; *P* = 0.034; Table 2). Maximal isokinetic muscle strength tended to be lower, and maximal isometric muscle strength was significantly lower in GHD patients compared to healthy controls (*P* = 0.06 and *P* = 0.002, respectively). Neither isokinetic nor isometric intrinsic muscle strength was significantly different between patients and healthy controls.

**Muscle bioenergetics.** The Pi/PCr, (PCr+Pi)/ATP, and Pi/ATP ratios were not significantly different between patients with GHD and healthy controls.

### TABLE 1. Correlation coefficients of isometric and isokinetic strength with several parts of the quadriceps volume, as determined by MRI

<table>
<thead>
<tr>
<th>Partial quadriceps vol</th>
<th>Isometric muscle strength</th>
<th>Isokinetic muscle strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trochanter major to patella</td>
<td>0.753</td>
<td>0.848</td>
</tr>
<tr>
<td>Trochanter minor to patella</td>
<td>0.759</td>
<td>0.851</td>
</tr>
<tr>
<td>Maximum volume (one slice)</td>
<td>0.818</td>
<td>0.889</td>
</tr>
<tr>
<td>5 slices around maximum</td>
<td>0.823</td>
<td>0.918</td>
</tr>
<tr>
<td>Midway (one slice)</td>
<td>0.735</td>
<td>0.843</td>
</tr>
<tr>
<td>Middle 9 slices</td>
<td>0.743</td>
<td>0.847</td>
</tr>
<tr>
<td>Sum of 10 slices below trochanter minor</td>
<td>0.837</td>
<td>0.932</td>
</tr>
<tr>
<td>Sum of 12 slices below trochanter minor</td>
<td>0.841</td>
<td>0.933</td>
</tr>
<tr>
<td>Sum of 14 slices below trochanter minor</td>
<td>0.835</td>
<td>0.929</td>
</tr>
</tbody>
</table>

**Childhood-onset vs. adult-onset GHD**

Adults with childhood-onset GHD (n = 7) had significantly lower isokinetic and isometric muscle strengths than adults with adult-onset GHD (n = 21; *P* = 0.008 and *P* < 0.0005, respectively). When the seven adults with childhood-onset GHD were compared with seven adult-onset GHD patients of comparable age, differences in strength remained significant. No significant differences were found when strength was corrected for the lower body height in patients with childhood-onset GHD.

Differences in muscle volume and intrinsic muscle strength between patients with childhood-onset and adult-onset GHD cannot be compared due to these differences in body height; a relatively larger part of the quadriceps was used in the determination of (partial) muscle volume in patients with childhood-onset GHD.

The (PCr+Pi)/ATP ratio was not significantly different between adult-onset (n = 13) and childhood-onset (n = 7) GHD patients (3.77 ± 0.08 and 3.59 ± 0.08, respectively; *P* = 0.178). The intracellular pH tended to be higher in patients with childhood-onset GHD than in those with adult-onset GHD (*P* = 0.069), and the Pi/PCr ratio was significantly lower in adults with childhood-onset GHD compared to adult-onset GHD patients (0.130 ± 0.007 and 0.150 ± 0.005, respectively; *P* = 0.026; Fig. 1). The Pi/PCr ratio remained significant when childhood-onset GHD patients were compared with seven adult-onset GHD patients of comparable age. Compared to healthy controls, no significant differences were found in (PCr+Pi)/ATP, pH, and Pi/PCr for both the childhood-onset and the adult-onset group, although childhood-onset patients tended to have low Pi/PCr, especially when one patient with a clubfoot and sequential changes in calf and knee-flexor muscles was excluded from the analysis.

**GH therapy**

**GH dose and serum IGF-I.** The mean GH dose after 1 yr of treatment was 1.3 ± 0.8 IU/day. The mean serum IGF-I concentration after 1 yr was 26.4 ± 1.2 nmol/L, which is in the high normal range (+1.5 ± 0.2 sd score). Seven of the 28 patients had levels of serum IGF-I above normal for age (> +2 sd score).

**Muscle volume and strength.** In Fig. 2, the percent change in muscle volume and isokinetic and isometric strengths is given. Muscle volume significantly increased (absolute change, 29.9 ± 7.3 cm³; *P* = 0.001). Isokinetic muscle strength also significantly increased, and isometric muscle strength tended to increase after 52 weeks of rhGH therapy (*P* = 0.001 and *P* = 0.055, respectively). No significant difference was found in either isokinetic or isometric intrinsic muscle strength.

The increase in muscle volume was significantly correlated with the increase in isometric muscle strength (r = 0.517; *P* = 0.020). No significant correlation between increase in muscle volume and the increase in isokinetic muscle strength was found. The percent increase in isometric muscle strength was significantly correlated with the percent increase in isokinetic muscle strength (r = 0.382; *P* = 0.049).
Muscle energetics. No significant differences were found between baseline and 52 weeks of rhGH treatment for the parameters measured by $^{31}$P-MRS in adults with GHD (n = 20). Also, no significant changes were found when childhood-onset and adult-onset GHD patients were analyzed separately.

Discussion

We showed that adults with GHD have low quadriceps volume and low isometric strength and tend to have low isokinetic muscle strength compared to age- and height-matched controls, which can all be increased by rhGH therapy given in doses of 0.6–1.8 IU/day. There was no difference in muscle energy store, as measured by $^{31}$P-MRS, between adults with GHD and healthy controls. In addition, muscle energy store did not change during rhGH therapy.

Several studies on muscle strength were performed in adults with GH deficiency, but only Cuneo et al. compared isometric muscle strength with the mass of the muscle tested (1, 2). They reported low quadriceps strength per quadriceps area at the midthigh level, as measured by CT in adults with GHD (1), which is not in agreement with the results of the present study that showed normal intrinsic strength in adults with GHD. In the present study, quadriceps volume was measured by (multiple slice) MRI, by which the determination of cross-sectional areas of individual muscles is more accurate than with CT scanning.

As the measurement of total quadriceps volume is time-consuming, we investigated whether using a part of the volume would be sufficient. The strongest correlation between strength and muscle volume in healthy controls was found when quadriceps volume was based on the sum of 12 slices below the lesser trochanter. This correlation was stronger than the correlation between quadriceps strength and total quadriceps volume, which suggests that the proximal part of the muscle influences muscle strength relatively more than the distal part of the quadriceps muscle. Intrinsic muscle strength is higher in those muscles containing relatively more fast, type II fibers than in those with slow, type I fibers (15, 16). Therefore, the present findings suggest that the proximal part of the quadriceps consist of relatively higher ratio of type II to I fibers than the distal part. The rectus femoris and vastus lateralis (both located relatively more proximally than distally) have a higher percentage of type II fibers than those with slow, type I fibers (15, 16). Therefore, the present findings suggests that the proximal part of the quadriceps consist of relatively higher ratio of type II to I fibers than the distal part. The rectus femoris and vastus lateralis (both located relatively more proximally than distally) have a higher percentage of type II fibers than the vastus medialis and intermedius (located relatively more distally), which thus fits with our suggestion (17, 18). The present finding also fits with the relatively larger increase in cross-sectional area of the more proximal part of the quadriceps after specific (knee extensions) strength training in young male subjects (19).

No correlation was found between body height and intrinsic muscle strength in eight healthy subjects. However, using only part of the quadriceps volume has the disadvantage that muscle strength expressed per unit muscle cannot be compared in short patients with that in tall patients be-
MUSCLE VOLUME, STRENGTH, AND BIOENERGETICS DURING rhGH

cause there are differences in the relative part of the muscle measured. It is thus important to match patients with controls for body height, as was done in the present study. A comparison between intrinsic muscle strength in childhood-onset GHD adults with that in adult-onset GHD patients or healthy controls was thus not possible due to the small body height in childhood-onset GHD patients. The present study is therefore not able to solve the question of whether the heterogeneity between childhood-onset and adult-onset GHD patients, which is described earlier with regard to several biochemical parameters (8, 20), also applies for (intrinsic) muscle strength.

The \( ^{31} \text{P}-\text{MRS} \)-measured ratio of Pi to PCr is considered to be a reflection of the cellular bioenergetic state and energy potential. A high ratio Pi to PCr at rest has been found in several (mitochondrial) myopathies. In addition, the (PCr+Pi)/ATP ratio is positively correlated with the percentage of type II fibers, as determined histochemically, in healthy young adults (21). The Pi/PCr and (PCr+Pi)/ATP ratios were not significantly different in adults with GHD compared to those in healthy controls. In addition, this ratio did not change during GH therapy. These results thus suggest that GH does not influence the muscle energy store and the fiber type distribution in adults with GHD, which is in agreement with the results based on most muscle biopsies studies in both childhood- and adult-onset GHD patients (22–24).

However, the ratio of Pi to PCr was significantly lower in patients with childhood-onset GHD compared to patients with adult-onset GHD. Moreover, this ratio tended to be lower in patients with childhood-onset GHD compared to healthy controls. Childhood-onset GHD patients could thus possibly have higher energy store. Rutherford (4) reported short half-relaxation time and rightward shift of force frequency relation of quadriceps muscle in patients (both childhood-onset and adult-onset) with GHD, which also point to a greater proportion of type II fibers within the muscle in adults with GHD. We thus conclude that if GH has an influence on muscle fiber types and the muscle energy store, it probably positively influences the ratio of type I to type II fiber area. A decrease in the intrinsic force in adults with GHD, as reported by Cuneo (1), was not confirmed in this study and is in contrast with the suggestions of the present bioenergetic results and the results of Rutherford (4).

The unchanged bioenergetics at rest in the total group of adults with GHD does not, however, rule out the possibility of abnormal changes in energy store during exercise and the recovery period, which reflect muscle efficiency and oxidative phosphorylation capacity. Several aspects limit the performance of exercise studies in the MR scanner. The ergometer should fit in the apparatus, and the materials used should not interfere with the magnetic field. Unfortunately, in our center we were (at that time) not able to perform exercise studies in the MR scanner. However, data are available after GHRH therapy for 6 weeks in healthy elderly men (25). No significant change was found in the PCr to PCr+Pi ratio or the pH of the muscle at rest, during exercise, or during recovery. In their relatively small study group in which the dose of GHRH was probably too low to significantly increase serum IGF-I concentrations, an increase in the aerobic reserve was postulated. They found a smaller (although nonsignificant) change in pH during exercise after GHRH therapy compared to pretreatment levels (25).

In agreement with the study by Johannsson (6), isometric muscle strength in the present study was low, and isokinetic muscle strength was in the low normal range in adults with GHD. The fact that isometric strength was relatively lower than isokinetic strength is in agreement with the results of the study by Rutherford et al. (4), who reported short half-relaxation time and rightward shift of force frequency relation of quadriceps muscle in patients with GHD.

Jørgensen et al. (26) performed a double blind, placebo-controlled study in patients with adult-onset GHD. They reported a significant increase in muscle strength and thigh muscle cross-sectional area in the GH treatment group, whereas a near-significant increase in muscle strength without a change in thigh muscle cross-sectional area was found in the placebo group. Jørgensen thus correctly notes that data on muscle strength in uncontrolled studies must be interpreted carefully. We cannot fully exclude that a training or placebo effect contributed to the increase in muscle strength in the present study, but the increase in muscle mass is likely to be a GH treatment effect. Moreover, the increase in muscle strength was related to the increase in muscle mass, as intrinsic muscle strength remained unchanged.

In the present study, voluntary maximal strength was measured. It could thus be possible that changes in a patient’s motivation or ability to perform maximal effort during rhGH treatment influenced the results of muscle strength. Johannsson et al. (6), however, applied a superimposed single twitch electrical stimulation test and found no reason to believe that the level of activation of motor units at voluntary maximal muscle effort was altered during the period of GH treatment.

In addition to the decreased muscle mass, GHD in adults is characterized by decreased psychological well-being, decreased maximal ventilation volume, decreased cardiac output, and increased fat mass, which can be reversed by rhGH treatment (27–29). Changes in these factors, however, could result in changes in the activity level. In the present study, no effort was made to influence a patient’s activity level during the study period. A questionnaire completed by the patient at baseline and after 52 weeks of treatment indicated that there were no major changes in sport activity, except in two patients, one of whom reported increased and one decreased sport activity. This result is in agreement with the results of others who measured activity by both a pedometer and detailed activity questionnaire (28).

It is notable that all except three patients with GHD had multiple pituitary deficiencies. Three of them had a history of hormone excess syndromes, such as ACTH excess (n = 1) or hyperprolactinemia (n = 2). Both hypo- and hyperfunction of the pituitary could influence muscle mass and strength, adding further complexity to the evaluation of these parameters in the deficient patients (30–32). In the present study, hyperfunction of the pituitary had occurred at least 10 yr ago. Moreover, all patients were receiving stable replacement therapy, if required, at least from 1 yr before the start of the study. No notable differences were found between the three patients with isolated GHD and the others.

We conclude that adults with GHD have reduced isomet-
ric muscle strength, which can be explained by reduced quadriceps muscle mass. Isokinetic muscle strength was relatively larger than isometric muscle strength in adults with GHD. During rhGH therapy, quadriceps strength increased in parallel with the increase in (partial) quadriceps volume, as determined by MRI.

Acknowledgments

The authors thank Mr. H. Lamb and Mr. F. Karstens for their assistance with this study.

References

7. Sartorio A, Narici M, Conti A, Monzani M, Fagiola G. 1995 Quadriceps and hand-grip strength in adults with childhood-onset growth hormone defi-

30. Wiles CM, Young A, Jones DA, Edwards RH. 1979 Muscle relaxation rate, fibre-type composition and energy turnover in hyper- and hypo-thyroid pa-

31. JANSSEN ET AL. JCE & M • 1999 Vol 84 • No 1