Longitudinal impact of aging on muscle quality in middle-aged men

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Abstract The present follow-up study aims at assessing the longitudinal changes in muscle quality after an interval of 9.45 years in middle-aged men. In addition, the relative contribution of muscle mass, muscle strength, and muscle power at middle age to these changes was investigated. The results showed a small, though unexpected, increase in total body and leg muscle mass (respectively 0.22 ± 0.04 and 0.29 ± 0.06 % yearly, $p < 0.0001$), whereas basic strength (-0.71 to -0.87 % yearly, $p < 0.0001$) and velocity-dependent strength and power (-1.19 to -1.86 % yearly, $p < 0.0001$) declined. Consequently, muscle quality, defined as the ratio of basic strength or velocity-dependent strength and power to muscle mass decreased (-1.46 to -2.43 % yearly, $p < 0.0001$) from baseline to follow-up. We found that baseline basic strength is a strong determinant of the decline in muscle quality basic strength with advancing age, whereas only a small part of the age-associated decline in muscle quality based on velocity-dependent strength and power could be explained. To conclude,

our results indicate that muscle becomes less efficient at middle age and that baseline muscle strength is a strong predictor of this change. These findings imply that unmeasured neural factors, influencing both contraction speed and the capacity of muscle to produce strength, are possibly other involved determinants. Therefore, timely interventions including strength training and higher-velocity strength training at middle age are recommended.

Keywords Sarcopenia · Dynapenia · Muscle function · Follow-up studies

Populations around the world are aging rapidly. These changing demographics highlight the importance to understand the modifiable risk factors for the loss of independence with advancing age. Previous studies found that poor physical performance was of major predictive value for the onset and development of disability (Guralnik et al. 2000; Singh 2002). In addition, it was observed that poor physical performance is closely linked with muscle mass, muscle strength, and muscle power (Singh 2002; Manini and Clark 2012). Since we rely upon skeletal muscle for every aspect of daily life, age-associated changes in these muscle characteristics became a topic of interest for both researchers and clinicians.

Aging men and women experience a decline in muscle mass and in muscle strength and muscle power, respectively defined as sarcopenia and dynapenia (Roubenoff and Hughes 2000; Clark and Manini

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2008). It is extensively reported that, based on cross-sectional data, muscle mass decreases with -1 to -2 % per year after the age of 50 (Frontera et al. 1991; Roubenoff and Hughes 2000; Macaluso and De Vito 2004). The age-associated losses in muscle strength, or the maximum force generation capacity, are even higher amounting from -1 to -1.5 % per year to -3 % per year after the sixth decade (Skelton et al. 1994; Macaluso and De Vito 2004; von Haehling et al. 2010). Additionally, aging seems to have a more detrimental impact on the ability to generate torque at higher movement velocities (Izquierdo et al. 1999; Lanza et al. 2003). In this regard, higher decline rates were observed for dynamic muscle strength compared to static muscle strength (Lanza et al. 2003). Moreover, muscle power is found to decline earlier and more precipitously than muscle strength (Macaluso and De Vito 2004; Kostka 2005). Starting at the age of 40 years, muscle power losses of -3 to -4 % per year are reported (Skelton et al. 1994). Finally, this mismatch between the age-associated changes in muscle mass, muscle strength, and muscle power suggests a strong decline in muscle quality with advancing age as well (Barbat-Artigas et al. 2012; Russ et al. 2012).

In geriatrics, muscle quality is more recently considered to be a clinically relevant determinant of physical performance and disability at older age (Barbat-Artigas et al. 2012). Consequently, a better understanding of the time course of the age-associated changes in muscle quality is crucial with regard to the prevention and treatment thereof. However, the abovementioned cross-sectional studies, investigating muscle characteristics across ages at a moment in time, cannot be used to establish causal relationships and to investigate the relative contribution of muscle mass, muscle strength, and muscle power to poor muscle quality at older age (Metter et al. 1997; Reid et al. 2014). Understanding the time course of the changes in muscle quality with advancing age thus requires a follow-up of the same individuals (Mitchell et al. 2012; Reid et al. 2014).

Yet, few studies with a longitudinal design investigated the relationship of muscle strength to muscle mass (Metter et al. 1999), and to the best of our knowledge, none of them addressed the relationship of muscle power to muscle mass. Also, this is the first longitudinal study using motor-driven dynamometry for the assessment of static and dynamic knee extension strength, as well as speed of movement of the knee extensors. To date, motor-driven dynamometry is considered the gold standard for measuring muscle strength (Osternig 1986;

Drouin et al. 2004). Furthermore, the long-term examination of muscle characteristics was often focused on old (>60 years) and very old adults (>80 years), thereby ignoring the changes in middle-aged adults (40–59 years). Nevertheless, previous data suggest that the detrimental impact of the aging process on muscle characteristics begins to occur at middle age. Additionally, given that the inclusion of a relatively homogeneous age sample may permit a clearer interpretation of the relationship between the age-associated changes, the longitudinal study of muscle quality in this select middle-age group may provide unique opportunities for prevention and timely interventions (Hofer et al. 2006).

Therefore, the present follow-up study aimed at assessing the initial longitudinal changes in muscle quality after an interval of 9.45 years in middle-aged men between 45 and 49 years of age at baseline. In addition, the relative contribution of muscle mass, muscle strength, and muscle power at baseline to these changes was investigated.

Methods

Subjects and study design

Subjects in the present study originally participated in the Leuven Growth Study of Belgian Boys (LGSBB) from 1969 to 1974, to evaluate physical fitness in Belgian boys between the ages of 12 and 18 years. The sampling procedure is previously described in detail by Matton et al. (2007). Shortly, a multistage cluster sampling procedure was chosen with schools as the primary sampling units. The first sampling stage resulted in the recruitment of 59 schools, selected following four stratification factors: language group (Dutch (Flemish) or French), type of schooling (vocational or humanities), school body (private or state), and geographic distribution of the school population over the nine Belgian provinces. In the second stage of sampling, entire classes were randomly selected from one grade of the secondary school. Since the same schools were visited each year, it was possible that boys previously enrolled in the study were re-selected in the following years. This selection could be considered random, as it was part of the design. In total, 588 boys were followed throughout the 6 years between 1969 and 1974. No selective drop-out was observed during this study. However, the boys that were followed each successive year were those who had

succeeded in their year of school. This might have introduced a systematic bias into the sample, given that all participants have finished secondary school.

In 1986, the LGSBB was extended and renamed the Leuven Longitudinal Study on Lifestyle, Physical Fitness and Health. Of the 588 boys followed over 6 years, 441 were Flemish speaking and were considered for further enrolment in this study. With the intention of five yearly follow-ups, the males were re-examined three times before they were contacted with regard to the baseline measurements of the present study in 2002–2004. Only those males that completed the previous measurements were contacted. An overview of the sample of the Leuven Longitudinal Study on Lifestyle, Fitness and Health is presented in a previous study of Matton et al. (2007).

With regard to the present study, 154 males between 45.39 and 49.67 years of age participated in the baseline measurements in 2002–2004. In 2012–2013, 105 participants (68.18 %) returned for follow-up measurements (see Fig. 1). They were screened on both occasions for medical history and had a physical examination and an electrocardiogram. Exclusion criteria were disorders that prohibit a maximal exercise test or a maximal strength test, such as severe cardiovascular disease, artificial hip or knee, acute hernia, infection, or tumor.

The study was approved by the University's Human Ethics Committee in accordance with the Declaration of Helsinki. All subjects gave written informed consent.

Main outcome measurements

Muscle mass

Muscle mass of both total body (MM_{TB} , g) and the right leg (MM_{LEG} , g) was assessed using dual-energy X-ray absorptiometry (DXA) by an expert radiologist at the university hospital. Muscle mass is defined as fat-free mass minus bone mineral content (Lee et al. 2001). Baseline measurements were performed with a QDR-4500A device, whereas a Discovery device was used for the follow-up measurements (Hologic, Waltham, MA, USA). Translation equations were developed in 26 adults between 23 and 80 years old to ensure comparability of the muscle mass measurements between both scanners. After cross-calibration, data obtained with the QDR-4500A device explained respectively 99.88 and

97.80 % of the variance of total body muscle mass and leg muscle mass obtained with the Discovery device.

Muscle strength and muscle power

Static and dynamic knee extension strength as well as speed of movement of the knee extensors was assessed with a Biodex Medical System 3[®] dynamometer (Biodex Medical Systems, Shirley, NY). Measurements were performed unilaterally on the right side, unless there was a medical contraindication. Participants were seated on a backward-inclined (5°) chair. The upper leg on test side and the hips and shoulders were stabilized with safety belts. The rotational axis of the dynamometer was aligned with the transversal knee-joint axis and connected to the distal end of the tibia using a length-adjustable rigid lever arm. Range of motion was set from a knee joint angle of 90° to 160° (a fully extended leg corresponds to a knee angle of 180°). Corrections for gravity were made by the Biodex software. The test protocol, including isometric, isotonic, and isokinetic tests, was run two times. The highest results were used for further analyses.

Static strength was assessed at a knee joint angle of subsequently 120° and 90°. Two maximal static knee extensions were performed in every knee joint angle. The peak torque (N m) of both contractions in both knee joint angles was recorded. Only the peak torque in 120° (STAT) was withheld for further analyses, whereas maximal isometric strength in 90° was used to set the external resistance during the isotonic tests.

Isotonic tests included three explosive knee extensions against a constant resistance of 20 % of the maximum isometric strength in a knee joint angle of 90°. The speed of movement (°/s) was recorded. The highest value of these three repetitions was defined as maximum speed of movement at 20 % (S_{20}).

Dynamic knee extension strength was assessed, conducting four knee extension-flexion movements at a low velocity of 60°/s and six repetitions at a high velocity of 240°/s. The peak torque (N m) of the knee extensions at respectively 60°/s (DYN_{60}) and 240°/s (DYN_{240}) was recorded.

Muscle quality

Muscle quality was calculated as the ratio of muscle strength or muscle power to leg muscle mass. Isometric (MQ_{STAT} , N m/g), isotonic (MQ_{S20} , °/s/g), as well as

Fig. 1 Participation flowchart of the study

isokinetic (MQ_{DYN60} and MQ_{DYN240} , N m/g) measures were normalized to MM_{LEG} .

Additional outcome measurements

Anthropometric measures

Body weight was measured to the nearest 0.1 kg using a digital scale (Seca, Hamburg, Germany). Height was measured to the nearest 0.1 cm using a portable anthropometer (GPM anthropological instruments, Zurich, Switzerland). Body mass index (BMI) was calculated (kg/m^2).

Aerobic fitness status

Aerobic fitness status was determined according to a maximal exercise test on an electrically braked Lode Excalibur cycle ergometer with gradually increasing intensity. The exercise test started at a load of 20 W, which was increased with 20 W every minute until volitional exhaustion. Oxygen consumption was measured using breath-by-breath respiratory gas exchange

analysis with a Cortex Metalyser 3B analyzer. Peak oxygen consumption (L/min), defined as the highest 20-s value during the exercise test, was used for statistical analyses.

Physical activity behavior

The Flemish Physical Activity Computerized Questionnaire (FPACQ), adapted for employed/unemployed people, was used to assess self-reported lifestyle and physical activity patterns. The FPACQ measures how much time each participant spent performing several physical activities during a normal week. The version for employed/unemployed people contains closed-ended questions on bouts of moderate and vigorous PA, total sedentary time, occupation, transportation in leisure time, watching TV or playing computer games, household chores, eating, and sleeping. The index used in the present study was the overall physical activity level index (PAL, metabolic equivalent (MET)), which was calculated as the summed energy expenditure of all reported activities divided by 168, the number of hours per week.

Statistical analyses

Data were expressed as means $\pm$ SEs. Equivalence between the original study population and the present study sample was assessed using two-sample *t* tests. In addition, significance of the changes in outcome parameters from baseline to follow-up was calculated. Since baseline measurements were spread over a period of 2 years and follow-up measurements were planned over 1 year, the follow-up period varied between subjects from 8.15 to 10.26 years, with a mean of 9.45 ± 0.04 years. Therefore, changes from baseline to follow-up in the outcome parameters were individualized and normalized per year. Significance of these changes was analyzed with paired sample *t* tests. Finally, stepwise linear regression was performed to investigate the relative contribution of baseline values to the longitudinal changes in muscle characteristics. The dependent variables included the longitudinal changes in muscle mass, muscle strength, muscle power, and muscle quality. The same, full set of baseline characteristics of body weight, muscle mass, muscle strength and muscle power, aerobic fitness status, and physical activity level, was introduced as potential predictors. In addition, scatter plots of the individual changes in muscle quality based on basic strength and basic strength at baseline were provided.

All analyses were performed using SPSS software version 19. Statistical significance was accepted as $p < 0.05$, using two-tailed tests.

Results

Baseline characteristics

A response rate of 68.18 % (105 participants) was reached (see Fig. 1). Of the other 49 participants, 14 participants could not be located and 9 participants did not respond. For individuals that refused returning for follow-up measurements, the main reasons cited were not interested ($n=12$), medical issues ($n=6$), and no time ($n=4$). In addition, data of four participants were not used in the statistical analyses because no baseline data were available ($n=2$) or they were excluded for follow-up measurements ($n=2$).

The baseline characteristics measured in 2002–2004 of the total sample that participated in the baseline measurements (total sample) as well as the sample that

returned for the follow-up measurements and thus was included in the present statistical analyses (follow-up sample) are presented in Table 1. When comparing the total sample with the follow-up sample used in the current study, no significant differences for any outcome parameters at baseline were present. Therefore, it is assumed that no selective drop-out occurred.

Longitudinal changes in the outcome parameters

Total body muscle mass as well as leg muscle mass significantly ($p < 0.0001$) increased from baseline to follow-up with respectively 0.22 ± 0.04 and 0.29 ± 0.06 % per year.

In contrast, muscle strength and muscle power significantly ($p < 0.0001$) decreased with annual losses of -0.87 ± 0.22 % in STAT, -0.71 ± 0.24 % in DYN₆₀, -1.19 ± 0.18 % in DYN₂₄₀, and -1.86 ± 0.15 % in S₂₀. The losses in S₂₀ were significantly larger compared with those in STAT ($p < 0.0001$), DYN₆₀ ($p < 0.0001$), and DYN₂₄₀ ($p = 0.003$). In addition, the losses in DYN₂₄₀ were significantly larger compared with those in DYN₆₀ ($p = 0.007$).

Consequently, muscle quality, defined as the ratio of muscle strength or muscle power to leg muscle mass strongly ($p < 0.0001$) decreased from baseline to follow-up. Annual losses of -1.62 ± 0.27 % in MQ_{STAT}, of -1.46 ± 0.24 % in MQ_{DYN60}, of -2.00 ± 0.18 % in MQ_{DYN240}, and of -2.43 ± 0.16 % in MQ_{S20} were found. In line with the above, losses in MQ_{S20} were significantly larger compared with those in MQ_{STAT} ($p = 0.007$), MQ_{DYN60} ($p < 0.0001$), and MQ_{DYN240} ($p = 0.046$). Additionally, the losses in MQ_{DYN240} were significantly larger compared with those in MQ_{DYN60} ($p = 0.006$).

Finally, body weight and BMI significantly increased with 0.13 ± 0.05 % per year ($p = 0.019$) and 0.15 ± 0.05 % per year ($p = 0.011$), respectively, whereas peak oxygen consumption and PAL index decreased with -0.39 ± 0.18 % per year ($p = 0.015$) and -0.17 ± 0.09 % per year ($p = 0.040$), respectively (Table 2).

Relative contribution of baseline values

Results from the stepwise linear regression analyses are presented in Table 3. Baseline parameters that contributed significantly to the longitudinal changes were shown. In addition, the relationship between the individual changes in muscle quality based on basic strength and basic strength at baseline is shown in Fig. 2.

Table 1 Baseline characteristics (means $\pm$ SE) measured in 2002–2004 of the total sample that participated in the baseline measurements (total sample) and the sample that returned for the follow-up measurements (follow-up sample)

	<i>n</i>	Total sample (<i>n</i> =154)	<i>n</i>	Follow-up sample (<i>n</i> =105)	<i>p</i> value ^a
Baseline muscle mass					
MM _{TB} (g)	149	61,756.38 $\pm$ 518.89	102	61,753.55 $\pm$ 639.36	0.997
MM _{LEG} (g)	149	9,966.87 $\pm$ 115.69	101	10,088.94 $\pm$ 116.53	0.474
Baseline muscle strength and power					
STAT (N m)	140	180.59 $\pm$ 3.53	99	183.10 $\pm$ 4.43	0.204
DYN ₆₀ (N m)	139	181.80 $\pm$ 3.16	98	183.70 $\pm$ 3.81	0.700
DYN ₂₄₀ (N m)	140	103.64 $\pm$ 1.78	98	104.91 $\pm$ 2.16	0.649
S ₂₀ (°/s)	140	405.89 $\pm$ 3.57	99	407.26 $\pm$ 3.76	0.797
Other outcome measures at baseline					
Age (years)	154	46.98 $\pm$ 0.05	105	46.93 $\pm$ 0.06	0.540
Body weight (kg)	154	81.51 $\pm$ 0.88	105	80.93 $\pm$ 1.01	0.666
Body height (cm)	154	177.76 $\pm$ 0.46	105	178.10 $\pm$ 0.53	0.629
BMI (kg/m ²)	154	25.79 $\pm$ 0.26	105	25.49 $\pm$ 0.28	0.437
Peak oxygen consumption (L/min)	142	2.97 $\pm$ 0.05	97	3.03 $\pm$ 0.06	0.323
PAL index (MET)	149	1.75 $\pm$ 0.01	103	1.74 $\pm$ 0.02	0.603

n number of subjects included in the measurements, *MM_{TB}* total body muscle mass, *MM_{LEG}* leg muscle mass, *STAT* static muscle strength, *DYN₆₀* dynamic muscle strength at a low velocity of 60°/s, *DYN₂₄₀* dynamic muscle strength at a high velocity of 240°/s, *S₂₀* speed of movement at 20 % of the static maximum strength, *BMI* body mass index, *PAL index* physical activity level index

^a Results from two-sample *t* tests

Results indicate that only a small percentage of the longitudinal changes in *MM_{TB}* could be explained by the predictors in our model, and no variables were entered into the equation regarding the changes in *MM_{LEG}* from baseline to follow-up.

The longitudinal changes in *STAT* are mostly determined by *STAT* at baseline. However, the *R*² value of baseline muscle strength and power to the longitudinal changes in *DYN₆₀* was lower and even further decreased with regard to changes in *DYN₂₄₀* and *S₂₀* from baseline to follow-up.

Similar findings were found for the longitudinal changes in *MQ_{STAT}* (see Fig. 2a), *MQ_{DYN60}* (see Fig. 2b), *MQ_{DYN240}*, and *MQ_{S20}*. In addition, Table 3 and Fig. 2 show a negative relationship between the longitudinal changes in muscle quality based on basic strength and basic strength at baseline.

Discussion

The present study assessed the age-associated changes in muscle quality over an interval of 9.45 years in middle-aged men between 45 and 49 years of age. To

the best of our knowledge, this is the first longitudinal study addressing the relationship of muscle strength and muscle power to muscle mass in this age group. A particular novel finding was that during the initial phase of the aging process, the strength- and power-generating capacity of muscle declines, despite a small, further increase in muscle mass. As a consequence, it is stated that muscle efficiency is lost at middle age, since a significantly lower amount of strength or power can be produced by the same, or even a slightly higher amount of muscle mass. Regression analyses revealed that the underlying determinants of these age-associated changes in muscle quality are mainly related to baseline muscle strength. These findings also imply that unmeasured neural factors, influencing both contraction speed and the capacity of muscle to produce strength, are additional important determinants.

In the present study sample of middle-aged men, rather small age-associated increases in body weight (0.13 % per year) and BMI (0.15 % per year) were found. Moreover, the present loss in aerobic fitness status of -0.39 % per year is also smaller compared to the evidence-supported -1.0 % per year (Hawkins and Wiswell 2003; Fleg et al. 2005). Nevertheless, since a

Table 2 Mean values ($\pm$ SE) at baseline and follow-up as well as absolute changes per year in main and additional outcome measures

	<i>n</i>	Baseline	<i>n</i>	Follow-up	Absolute changes per year	<i>p</i> value ^a
Main outcome measures						
MM _{TB} (g)	102	61,753.55 $\pm$ 639.36	90	63,066.99 $\pm$ 722.95	140.43 $\pm$ 23.01	<0.0001
MM _{LEG} (g)	101	10,088.94 $\pm$ 116.53	90	10,428.74 $\pm$ 136.33	29.93 $\pm$ 5.69	<0.0001
STAT (N m)	99	183.10 $\pm$ 4.43	82	159.48 $\pm$ 3.50	-2.06 $\pm$ 0.41	<0.0001
DYN ₆₀ (N m)	98	183.70 $\pm$ 3.81	82	163.35 $\pm$ 4.10	-1.62 $\pm$ 0.43	<0.0001
DYN ₂₄₀ (Nm)	98	104.91 $\pm$ 2.16	82	89.43 $\pm$ 1.96	-1.37 $\pm$ 0.19	<0.0001
S ₂₀ (°/s)	99	407.26 $\pm$ 3.76	82	331.77 $\pm$ 5.64	-7.60 $\pm$ 0.60	<0.0001
MQ _{STAT} (Nm/g)	96	0.021 $\pm$ 0.002	70	0.012 $\pm$ 0.0003	-0.0004 $\pm$ 0.00005	<0.0001
MQ _{DYN60} (Nm/g)	95	0.018 $\pm$ 0.0003	70	0.015 $\pm$ 0.0003	-0.0003 $\pm$ 0.00004	<0.0001
MQ _{DYN240} (Nm/g)	95	0.010 $\pm$ 0.0002	70	0.008 $\pm$ 0.0002	-0.0002 $\pm$ 0.00002	<0.0001
MQ _{S20} (°/s g ⁻¹)	96	0.041 $\pm$ 0.0006	70	0.031 $\pm$ 0.0008	-0.0010 $\pm$ 0.00007	<0.0001
Additional outcome measures						
Body weight (kg)	105	80.93 $\pm$ 1.01	103	81.94 $\pm$ 1.12	0.10 $\pm$ 0.04	0.019
Body height (cm)	105	178.10 $\pm$ 0.53	103	177.90 $\pm$ 0.54	-0.02 $\pm$ 0.01	0.003
BMI (kg/m ²)	105	25.49 $\pm$ 0.28	103	25.85 $\pm$ 0.30	0.04 $\pm$ 0.01	0.011
Peak oxygen consumption (L/min)	97	3.04 $\pm$ 0.06	79	2.94 $\pm$ 0.07	-0.02 $\pm$ 0.01	0.015
PAL index (MET)	103	1.74 $\pm$ 0.02	100	1.71 $\pm$ 0.02	-0.003 $\pm$ 0.002	0.040

n number of subjects included in the measurements, *MM_{TB}* total body muscle mass, *MM_{LEG}* leg muscle mass, *STAT* static muscle strength, *DYN₆₀* dynamic muscle strength at a low velocity of 60°/s, *DYN₂₄₀* dynamic muscle strength at a high velocity of 240°/s, *S₂₀* speed of movement at 20 % of the static maximum strength, *MQ_{STAT}* muscle quality based on static muscle strength, *MQ_{DYN60}* muscle quality based on dynamic muscle strength at a low velocity of 60/s, *MQ_{DYN240}* muscle quality based on dynamic muscle strength at a high velocity of 240°/s, *MQ_{S20}* muscle quality based on speed of movement at 20 % of the static maximum strength, *BMI* body mass index, *PAL index* physical activity level index

^aResults from paired sample *t* tests

PAL index of 1.7 indicates a physically active lifestyle and is found to be associated with the maintenance of body weight within a healthy BMI range, a smaller impact of the aging process on these outcome measures could be expected (Saris et al. 2003; Brooks et al. 2004). In addition, the present study sample was found to be representative for the population of Flemish males regarding body composition and physical activity. Only socioeconomic status was above average (Matton et al. 2007).

Our data of a DXA scan revealed an increase in both total body muscle mass and leg muscle mass of respectively 0.22 and 0.29 % per year. However, it is widely reported that, based on cross-sectional data, muscle mass decreased with -1 to -2 % per year after the age of 50 years. Moreover, the few longitudinal studies that assessed estimates of muscle mass over time also reported a decline with advancing age. Depending on the assessment techniques, the duration of the follow-up period and the population studied, a wide range of

annual losses between -0.02 and -1.29 % and between -0.07 and -1.34 % was found for estimates of respectively total body muscle mass (Guo et al. 1999; Hughes et al. 2001, 2002; Fantin et al. 2007) and leg muscle mass (Frontera et al. 2000, 2008; Goodpaster et al. 2006; Fantin et al. 2007; Delmonico et al. 2009; Koster et al. 2011; Kitamura et al. 2014) in men and women aged 40 to 81 years. However, the former studies included study populations with a wider age range, including older birth cohorts. Kitamura et al. (2014), on the other hand, assessed 6-year longitudinal changes in total body muscle mass measured by DXA and divided their study population into narrow age cohorts. They also found a small, but significant increase in total body muscle mass of 0.27 % per year in men in their 40s and of 0.12 % per year in men in their 50s. In addition, cross-sectional analyses of Kyle et al. (2001) reported that muscle mass peaked between 35 and 59 years in men, suggesting that the age-associated muscle atrophy starts in the latter portion of the fifth or sixth decades.

Table 3 Stepwise linear regression analyses with the longitudinal changes in muscle function as dependent variables and baseline characteristics as independent variables

	ΔMM_{TB}	ΔMM_{LEG}	$\Delta STAT$	ΔDYN_{60}	ΔDYN_{240}	ΔS_{20}	ΔMQ_{STAT}	ΔMQ_{DYN60}	ΔMQ_{DYN24}	ΔMQ_{S20}
Predictors	Standardized β									
	<i>F</i> of change									
Body weight (kg)				0.28**						
				4.71						
MM_{TB} (g)						-0.34*				-0.33*
						9.45				7.39
STAT (N m)			-0.72*				-0.73*			
			37.29				36.85			
DYN_{60} (N m)	-0.47*		0.28*	-0.45*			0.29*	-0.56*		
	4.55		7.23	18.29			7.42	27.88		
DYN_{240} (N m)	0.71*				-0.39*				-0.41*	
	7.22				12.51				12.75	
Adjusted R^2	0.12	.	0.39	0.23	0.14	0.11	0.42	0.30	0.16	0.09

ΔMM_{TB} change in total body muscle mass, ΔMM_{LEG} change in leg muscle mass, $\Delta STAT$ change in static muscle strength, ΔDYN_{60} change in dynamic muscle strength at a low velocity of 60°/s, ΔDYN_{240} change in dynamic muscle strength at a high velocity of 240°/s, ΔS_{20} change in speed of movement at 20 % of the static maximum strength, ΔMQ_{STAT} change in muscle quality based on static muscle strength, ΔMQ_{DYN60} change in muscle quality based on dynamic muscle strength at a low velocity of 60/s, ΔMQ_{DYN240} change in muscle quality based on dynamic muscle strength at a high velocity of 240°/s, ΔMQ_{S20} change in muscle quality based on speed of movement at 20 % of the static maximum strength

* $p < 0.010$, significant; ** $p < 0.033$, significant

In contrast, the present study found that muscle strength and muscle power decreased from baseline to follow-up in middle-aged men. Decline rates in basic strength, including static strength and dynamic strength at low speed, ranged from -0.71 to -0.87 % per year.

The age-associated losses in velocity-dependent strength, including dynamic strength at high speed and speed of movement, are markedly larger compared to those in basic strength, ranging from -1.19 to -1.86 % per year. According to previous findings, the more

Fig. 2 Relationship between the individual changes in muscle quality based on basic strength (in % per year) and basic strength at baseline. More specifically, in **a** the relationship between muscle quality based on static strength and static strength at baseline is

presented, whereas **b** shows the relationship between muscle quality based on dynamic strength at a low velocity of 60°/s and dynamic strength at a low velocity of 60°/s at baseline

detrimental impact of the human aging process on dynamic muscle strength and muscle power is related to the age-associated slowing of contraction speed (Lanza et al. 2003; Macaluso and De Vito 2004; Raj et al. 2010). However, former longitudinal research in aging men and women between 46 and 85 years consistently reported higher decline rates (-1.18 to -3.42 % per year) in muscle strength and muscle power compared to the present study (Frontera et al. 2000; Hughes et al. 2001a; Goodpaster et al. 2006; Delmonico et al. 2009; Hicks et al. 2012; Reid et al. 2014). In contrast to this research, this study included only middle-aged adults and applied a narrow age range (45–50 years at baseline) to focus on the changes during the initial phase of the aging process (Hofer et al. 2006). Therefore, our results support previous cross-sectional findings, suggesting a nonlinear decline in muscle strength and muscle power, with small initial losses that accelerate thereafter (Skelton et al. 1994; Macaluso and De Vito 2004; von Haehling et al. 2010).

The abovementioned temporal discrepancies observed in the age-associated changes in muscle mass, muscle strength, and muscle power point toward the importance of the wider concept of muscle quality. Muscle quality is defined as the ratio of basic strength or velocity-dependent strength and power to muscle mass and is found to strongly decrease from baseline to follow-up, ranging from -1.46 to -2.43 % per year. As a consequence, it can be stated that muscle efficiency is lost at middle age, since a significantly lower amount of strength or power can be produced by the same or even a slightly higher amount of muscle quantity. These results are in line with previous studies, indicating that even a gain in muscle mass does not prevent the loss of muscle strength and muscle power (Hughes et al. 2001; Goodpaster et al. 2006). Furthermore, it is suggested that neural factors deteriorate earlier and more precipitously compared to muscle quantity (Frontera et al. 2000; Goodpaster et al. 2006; Delmonico et al. 2009; Reid et al. 2014). This dissociation implies that other factors than muscle mass play a role in the onset and progression of the age-related changes in muscle quality (Metter et al. 1997; Clark and Manini 2008; Reid et al. 2014).

To gain a better insight in the initial age-associated course of the present changes in muscle quality, the relative contribution of muscle mass, muscle strength, and muscle power at middle age was further examined. First, the level of muscle mass at middle age did not

contribute to the longitudinal changes in muscle quality based on basic strength and only barely contributed to the longitudinal changes in muscle quality based on velocity-dependent strength and power. This finding supports the dissociation between muscle quantity and neural factors, as mentioned earlier. In addition, former research found that the changes in muscle mass only explain ~ 5 to 8 % of the variability in muscle strength. In contrast, we observed that baseline basic strength is a strong determinant of the decline in muscle quality based on basic strength with advancing age, explaining 30 to 42 % of the observed interindividual variation. Correspondingly, results of Rantanen et al. (1998) also indicate that more than 30 % of the variation in handgrip strength measured in older adults is explained by midlife strength. However, we found that stronger men at baseline experience larger longitudinal losses in muscle quality based on basic strength. Similar results were observed in a study population of older men between 70 and 79 years old (Goodpaster et al. 2006). They suggested that selection bias might have attenuated the longitudinal losses, as weaker participants did not return for the follow-up measurements. Correspondingly, the present study included only healthy, physically active men at middle age. It is possible that greater losses in muscle strength and power would have been found in weak, inactive participants at baseline. In addition, we cannot exclude the possibility that stronger men at baseline lost more muscle quality due to a regression toward the mean.

With regard to the age-associated decline in muscle quality based on velocity-dependent strength and power on the other hand, only a small part of the changes could be explained by midlife velocity-dependent strength and power. This finding emphasizes the importance of additional factors, including unmeasured neural factors influencing both contraction speed and the capacity of muscle to produce strength, as determinants in this decline (Metter et al. 1997; Clark and Manini 2008; Reid et al. 2014). Recent cross-sectional data in middle-aged men indicate no age-associated loss in rapid muscle activation, which may be affected by motor unit recruitment, firing, and discharge rates (Clark et al. 2011; Thompson et al. 2013). However, it is speculated that the initial stages of motor unit remodeling, occurring early in the fifth decade, may result in a loss of muscle efficiency at middle age (Lexell et al. 1986; Thompson et al. 2013). More specifically, the number of functioning motor units decreases during

aging, with an accelerated loss of fast motor units. Reinnervation of the denervated fibers by the remaining motor units ends in a net conversion of fast type II muscle fibers into slow type I muscle fibers, thereby compromising the strength- and power-generating capacity of muscle (Lexell et al. 1986; Rolland et al. 2008). In addition, the increased co-activation of antagonist muscles seen in older adults is highlighted as a potential mechanism (Macaluso et al. 2002; Bautmans et al. 2011). On the other hand, the contribution of the age-associated changes in muscle architecture has seldom been considered. Nevertheless, a reduced fiber fascicle length and a smaller pennation angle could also affect the force- and power-generating capacity of muscle (Narici et al. 2003).

The identification of midlife strength as early determinant of the age-associated decline in muscle quality may provide opportunities for timely interventions in the prevention of low muscle quality at older age. However, results from both the present and previous studies (Hughes et al. 2001; Stenholm et al. 2012) suggest that general physical activity may not be effective enough to prevent the age-associated decline in muscle quality at middle age. Therefore, it is stated that more specific training is required. Based on the present losses observed in basic strength and velocity-dependent strength and power, strength training and higher-velocity strength training interventions at middle age might be recommended.

The following limitations of the present study should be acknowledged. First, although a rather high response rate of 68.18 % was reached, our sample size was rather small. In addition, only men were included. Second, present study sample can be considered representative for the population of Flemish males (Matton et al. 2007), except for socioeconomic status. The latter might compromise the generalizability of the present results. In addition to their higher socioeconomic status, participants of the present study were mostly healthy and physically active. Therefore, our results may underestimate the age-associated changes in muscle characteristics at middle age. Third, the FPACQ only addressed the past year's physical activity recall. However, lifetime physical activity may have a stronger impact on muscle function than more recent habits (Hughes et al. 2001). Finally, given the operational life span of a DXA scanner, the device used at baseline had to be replaced. Consequently, baseline measurements and follow-up measurements were performed with a different device.

Nevertheless, translational equations were developed to ensure comparability of the muscle mass measurements between both scanners.

Conclusion

Our results indicate that although the quantity of muscle even further increased in middle-aged men, its strength- and power-generating capacity strongly declined. Consequently, muscle becomes less efficient at middle age. The present study designates baseline muscle strength as a predictor of this age-associated loss of muscle quality. These findings also imply that other unmeasured neural factors, influencing both contraction speed and the capacity of muscle to produce strength, are involved in this loss of muscle quality. Given the importance of muscle quality for physical performance, prevention of its age-associated decline through timely strength training and higher-velocity strength training interventions at middle age is recommended.

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