Muscle force, balance and falls in muscular impaired individuals with myotonic dystrophy type 1 - A five-year prospective cohort study.

Authors: Elisabet Hammarén[a,b,c], Gunilla Kjellby-Wendt[a,c], Christopher Lindberg[b,c]

[a]Physiotherapy Department, Sahlgrenska University Hospital, Gothenburg, Sweden

[b]Neuromuscular Centre, Sahlgrenska University Hospital, Gothenburg, Sweden

[c]Sahlgrenska Academy at the University of Gothenburg, Institute of Neuroscience and Physiology, Dept of Clinical Neuroscience, Gothenburg, Sweden

Corresponding author:

Elisabet Hammarén, PT, MSc

Physiotherapy Department, Sahlgrenska University Hospital, Vita stråket 13,

S-413 45 Gothenburg, SWEDEN

Phone: +46 (31) 3428898, Fax: +46 (31) 7765532

Email: elisabet.hammaren@vgregion.se (can be published)

Gunilla Kjellby-Wendt, PT, PhD, Physiotherapy Dept. Manager, Mölndal, Sahlgrenska University Hospital, Sweden. Email: gunilla.kjellby-wendt@vgregion.se

Christopher Lindberg, MD, PhD, Associate Professor at the Institute of Neuroscience and Physiology, Dept of Clinical Neuroscience, Sahlgrenska Academy at the University of Gothenburg, Sweden. Email: christopher.lindberg@vgregion.se

Abstract

Individuals with myotonic dystrophy type 1 (DM1) have progressive muscle weakness with gait and balance impairments. We explored prospectively the natural history of muscle force, gait, balance, balance confidence and walking ability in muscular affected individuals with DM1. After five years data from 43 individuals (m/f:18/25) were analysed. All measures of balance showed statistically significant deterioration (p<0.001) with averaged yearly loss of function by 3-4%. In the group as a whole, loss of muscle force was statistically significant in all lower limb muscles measured after five years: changes relative baseline force were median -6% to -18%. For males muscle force loss was statistically significant in all leg muscles, but only in hip flexors for women. After five years 100% of the men had fallen during previous year and 67% three times or more, in contrast only 60% of the women had fallen in the previous year and 36% three times or more. The proportion of individuals searching medical care the previous year after falling was more than doubled after five years, albeit the number of falls had not changed. Awareness of this increased risk of falls is important for caregivers and patients.

Keywords: Myotonic dystrophy; observation; self-reported falls; postural balance; muscle strength; physiotherapy.

1 Introduction

Myotonic dystrophy type 1 (DM1) is an inherited neuromuscular disorder with the highest prevalence among adults, 9-18/100.000 inhabitants [1, 2]. Functional impairments in multiple organ systems are common, including cognitive deficits and fatigue [3, 4]. Myotonia and/or muscle weakness in the distal muscles of the leg and arm are the main characteristics of the muscle affection in individuals with DM1 [3].

In individuals with DM1 an increased risk of stumbles and falls has been shown [5]. The main factor for this is suggested to be the slowly progressive weakness in the leg muscles [5]. The cognitive deficits and the fatigue [6] could contribute to the impaired postural control resulting in frequent stumbles and falls. There is a need for a closer knowledge of the evolvement of the balance impairment and falls of the individual with DM1.

Only a few studies of the progression of muscle weakening and impairments in individuals with DM1 have been conducted [7-11]. By using manual muscle testing an average decline of 0.95% per year in muscle strength has been shown in a cross-sectional study of 50 individuals with DM1 [7]. The study evaluated muscle strength loss per year of disease duration. The decline was more rapid in the distal muscles with no significant difference between genders (0.99% in females and 1.54% in men per year). The same study evaluated muscle force with quantitative measurements using dynamometry in hand grip, lateral pinch, elbow extensors, hip flexors and ankle dorsiflexors, showing a decline of 1% (elbow extensors in females) to 3% (hand grip in men) per year of disease duration. Furthermore, a gender effect noted was that women were weaker than men in all muscles [7]. Hand grip, lateral pinch and neck muscle force have been evaluated in a longitudinal study over two years with dynamometry and strain gauge, showing very small but significant force increases, that according to the authors probably are due to normal variations or a training effect [8]. All other muscles were evaluated with manual muscle testing, through full range, and showed a strength decline [8]. Another longitudinal study, with 158 consecutive individuals with DM1, showed a decline in handgrip force of 1.18kg/year in women and 1.61 kg/year in men [9]. A ten year prospective evaluation of 75 patients with non-congenital and 17 patients with congenital myotonic dystrophy showed a generalised weakness in both types, but progressive in the non-congenital type, only [10]. When performing a selenium-vitamin E study on patients with myotonic dystrophy, the authors concluded that a useful set of measurements to follow functional deterioration in this disorder would be hand-grip strength and maximal walking speed [11]. To our knowledge no prospective study on performance-based measures of balance in connection with leg muscle force using handheld dynamometry has been performed in individuals with DM1.

A prior mapping study including balance confidence, performance-based measures of balance, leg muscle force, walking and number of falls confirmed the increased risk of falling [12]. One factor of importance for increased number of falls was shown to be muscle weakness. A still remaining question is the natural course of the physical impairments. This is important for future studies on intervention effects in individuals with DM1.

The objectives of this study were to explore, in muscular impaired individuals with DM1, the natural history in muscle force, gait and performance-based measures of balance, as well as patient reported balance confidence, falls and walking ability.

2 Patients and Methods

2.1 Patients

All 72 eligible individuals with genetically proven DM1 at the Neuromuscular Centre, Sahlgrenska University Hospital, were invited by letter and/or by phone call to participate in a cross-sectional study [12]. All fifty-one patients who participated in this cross-sectional study were available for the present longitudinal study. In the previous study the inclusion criteria were: genetically confirmed non-congenital DM1 diagnosis; age between 20-60 years; and ability to perform Timed Up & Go (TUG) [13]. The exclusion criterion was other disorder that could affect postural control. Exclusion criteria for the present study were: (1) MIRS grade 1 or 2 (see part 2.3) or (2) inability to perform TUG in less than 30 seconds at baseline. The reason for the former criterion was that patients with MIRS 1 and 2 have the mild form of DM1 and thus have very little muscle symptoms. The mild form of DM1 is also reasonably stable over time, in our experience. The reason for the TUG criterion was that this cut-off in elderly individuals distinguishes between individuals dependent or independent in basic transfers [13]; and that patients walking so slowly would be likely to be a wheelchair user in a three year perspective , and need other forms of support. These narrowed criteria were due to the interest in postural control evaluation of weak but still independently ambulant patients, at risk for falls. Data from the mapping study was used as baseline data in the present study. The patients gave their written informed consent to participate in the study and knew that they could refuse further participation without any impact on further treatment. The Regional Ethical Review Board in Gothenburg, Sweden approved the study (Dnr 248-06 and Dnr 601-11).

2.2 Procedures

An experienced physiotherapist (EH), although having met some of the patients in the clinic during the five years, examined all patients at baseline and after five years, blinded to previous results. The self-assessments and the performance-based measures of balance were performed in a standardised order; first the self-assessments followed by the physical examinations. The examiner demonstrated the positions in the balance tests. Resting pauses were allowed and encouraged. The timing was performed with an electronic stopwatch with an accuracy of 1/100 second.

2.3 Measurements and assessments

An assessment and classification with Muscular Impairment Rating Scale (MIRS) was performed

[14]. The **MIRS** is an ordinal scale with five grades, with the definitions of the grades as follows: 1 - no muscular impairment; 2 - minimal signs, as ptosis and nasality, no distal weakness except digit flexor weakness; 3 - distal weakness, no proximal weakness except in elbow extensors; 4 - mild to moderate proximal weakness; and 5 - severe proximal weakness. For a more detailed definition see the original paper [14].

The **isometric muscle force** was assessed by the maximal amount of resistance in an isometric muscle effort with a handheld gauge meter (Mecmesin Basic Force Gauge 1000N, Chauvin Arnaux Group), and was recorded in newtons (N). The "break" method according to Phillips [15] and Bäckman [16] was used. The assessed muscle groups in this study were the hip flexors, knee extensors, knee flexors and the ankle dorsiflexors. The hip flexors and ankle dorsiflexors were assessed in supine position, according to Phillips [15], and the calf was supported with a pad during the ankle dorsiflexor assessment to get a free calcaneus. The knee extensors were measured in the sitting position, and the knee flexors were measured in the prone position, according to Bäckman [16]. The test-retest reliability of the handheld dynamometry in patients has been reported to Pearson's r 0.96 to 0.99 for the same muscle groups as was measured in the present study [17] and ICC 0.91-0.97 in another study in individuals with spinal muscular atrophy [18].

Timed 10-m walk (10mMAX): Walking at maximum speed was measured in a long corridor with an even surface over 10 meters with a still-standing start and a "flying" finish to a target 2.5 meters beyond the mark at 10 m [19-22]. The stopwatch was started on the word "Go" ("Ready-Steady-Go"). The patients were instructed to take their shoes and callipers off to minimize the risk of shoe difference bias at follow-up. The patients could choose to walk barefoot or in socks. An exception was made to allow AFO use when this was the only possible way a patient could walk 10 meters. Handheld walking aids were allowed when needed. All patients were well acquainted with the test. The test has shown test-retest stability in individuals with DM1 (ICC 0.94) [23].

Timed Up & Go (TUG): The patient rose with arm support from a seated position in a chair of normal height (44-45cm) with arms, walked at a comfortable and safe pace to a mark on the floor 3 meters away, turned, walked back to the chair, turned and sat down [13]. Handheld walking aids were allowed if needed. The test was performed twice with the second trial recorded. The test has shown test-retest stability in individuals with DM1 (ICC 0.83) [23].

Step test (STEP) was performed according to Hill et al [24]: The patient stood unsupported 5cm in front of an 8cm high block (40x40cm) and made as many “full steps” as possible during 15 seconds. One step comprised of placing one foot fully up onto and then down off the block. Both legs were tested, one foot at a time. The patient was allowed some practice steps and then one test attempt per leg. If balance was lost during the trial the completed steps were reported. The examiner kneeled by the block and held it to ensure it remained steady during the test. The test has shown test-retest stability in individuals with DM1 (ICC 0.83-0.94) [23].

The balance confidence was assessed by the **Activities-specific balance confidence (ABC)** scale [25] which consists of 16 items including both indoor and outdoor activity questions. The patient answered the question “How confident are you that you can maintain your balance and remain steady when you (...do X activity...)”. The score of each question was from 0 (no confidence) to 100 (full confidence) and the mean of the 16 items was used as a sum score [25]. After contact with Dr Myers (the original constructor), a forward and backward translation to the Swedish language was made and used with her permission. The test has shown test-retest stability e.g. in patients with Parkinsonism (ICC 0.94) [26].

A self-report questionnaire of walking ability, **Reported walking index (RW-index)** [27], was used. It consists of five items concerning walking balance, walking difficulty indoors/outdoors and the use of walking aids. Two items have possible scores from one to three, the other three are dichotomous (yes/no). When use of walking aids was confirmed, the patients were also asked to report what type of aids they used, e.g. ankle-foot orthoses and walking sticks. The maximum total score is 12, showing no subjective walking difficulties, the minimum score is 5 showing very large walking difficulties. The RW-index has shown concurrent validity with a number of clinical tests of balance and walking. It has also proved to be a statistically significant predictor of falls and fractures [28].

The patients were asked semi-structured **questions on falls**: how many unintentional falls during the previous year they had experienced; how it happened; if the falls had resulted in any injuries; and if any medical care was needed. If the number of falls were too many to actually remember, some memory cues were provided to assist the patient in estimating number of falls based on incidents during the last week and month. They were also asked if they were afraid of falling (yes/no) and if they avoided activities due to fear of falling (yes/no). The World Health Organization fall definition was used: "an event, which results in a person coming to rest inadvertently on the ground or floor or other lower level" [29].

2.4 Statistics

To show the sometimes skewed distribution the continuous variables are presented both as mean and standard deviation (SD) as well as median and minimum-maximum (min-max). The categorical data is shown as number and percentage. For muscle force and Step test measurements, as no significant differences could be detected between right and left side values, the mean of the two sides was used in the analysis. When data was missing at year five (Y5), the missing data was substituted with the three-year data for these individuals. A dichotomisation of the categorical variable RWI for further analysis was performed using a cut-off for equally large subgroups. Changes over time were analysed with the Wilcoxon Signed rank test for continuous variables, and for categorical and dichotomous variables with Sign test. For comparison between two groups Mann Whitney U test was used for continuous variables, and Mantel-Haenszel Chi Square Exact test for ordered categorical variables. All significance tests were two-sided at the 5% significance level. The Spearman's rang correlation was used for correlation analysis. Calculations were made in SPSS®, Statistics, v20 (IBM, USA) and SAS software, Version 9.

3 Results

3.1 Patients

Forty-six patients were included at baseline in the present study group (Figure 1). After three early dropouts due to far relocation and disease progress, the results of the assessments are based upon 43 patients; 25 women and 18 men, mean (SD) age 41 (9.4) years, with body mass index (BMI) mean (range) 24.4 (17.2-37.5) kg/m^2, at baseline. In the five-year assessment, 41 of the initial patients participated, and for the two remaining patients their missing data at Y5 were replaced with their available three-year data. The reason for drop-out at year five was worsening of the disease. Table 1 shows the baseline characteristics of the included patients and the early dropouts. At Y5 the mean (range) in BMI was 25.6 (17.5-39.4) kg/m^2.

3.2 MIRS

The distribution of patients in each MIRS impairment grade was significantly changed (p<0.001) at Y5: no men or women had become better, but seven men (39%, p=0.016) and six women (24%, p=0.031) had become worse.

3.3 Isometric muscle force

After five years a statistically significant muscle force loss was shown in each measured muscle group between the baseline observation and Y5, Table 2. For the whole group, the decline was most pronounced in the ankle dorsiflexor muscles, with a mean decrease of 12%. The other muscle groups had a mean decrease of 5-8% in five years. The individual variations, however, were large.

When the muscle force change was evaluated individually in relation to each patients' baseline force, the median decrease for the ankle dorsiflexors was 18%, p=0.002. For the other muscle groups the median decrease was 6-8% in five years, the probability value varying from p=0.023 in knee extensors to p<0.001 in hip and knee flexors.

Male individuals had a more pronounced reduction in all muscle groups except for the hip flexors, Figure 2. While the raw data only showed a statistically significant difference between genders in the absolute changes of knee extensors (p=0.019) and knee flexors (p=0.021), Table 2, the Mann-Whitney U analysis of relative change with respect to baseline force showed a statistically significant difference between genders also in the ankle dorsiflexors (p=0.034), Figure 2.

3.4 Timed 10-m walk, TUG and Step test

At the five-year assessment, Timed 10-m walk, TUG and Step test showed a statistically significant (p<0.001) deterioration compared to baseline, Table 2. The mean time in timed walk increased from 7.5 seconds at baseline to mean 9.3 seconds at Y5. At baseline males had longer time in 10mMAX, mean (SD) 8.1 (2.3) seconds vs. 7.1 (2.4) seconds in females. The deterioration was twice as large in males as in females: 2.5 (3.2) seconds vs. 1.2 (1.7) seconds, Table 2. The number of patients requiring shoes with AFO's to walk 10 m had increased from one to four, in addition two patients needed stabilising shoes without AFO's and two patients now used a rollator, or wheeled walker. In TUG the time increased from mean 9.6 to 12.0 seconds, Table 2. At baseline males had longer time, mean (SD) 10.1 (2.1) seconds compared to females, 9.3 (2.6) seconds. The deterioration was in males somewhat larger than in females 3.0 (4.8) seconds vs. 1.9 (3.5) seconds, Table 2. The number of steps in Step test was reduced with mean 2.5 steps or 19%, Table 2. However, none of the differences between genders were statistically significant. . The absolute changes in the performance-based measures of balance showed a statistically significant moderate correlation with the relative changes of force in the knee and ankle muscles, Table 3.

3.5 Self-assessment of balance confidence (ABC)

The results of the self-assessments are shown in Table 2. The Activities-specific Balance Confidence sum score had decreased, mean (SD) decrease -7 (18) units (p=0.024). The decrease was 10 units or more in 17 of the patients (40%). At baseline the ABC score for these patients did not differ from the other group.

3.6 Reported walking index (RW-index)

The study showed a statistically significant increase in reported walking difficulties after five years. Walking difficulties as indicated by RW-index ≤11, was reported by 70% of the patients at baseline, compared to 86% at Y5. A worsened walking ability was reported by 56% of all patients after five years. However, within the male group 67% reported a worsened walking ability. A dichotomisation into two equally large subgroups was made; RW-index “9 or lower”, versus RW-index “10 or higher”. In the group with lower (worse) self-reported walking ability, (n=21), 95% of the patients had fallen the previous year, median (range) number of falls 5 (0-13); versus 59% in the group with higher (better) walking ability (n=22), median (range) number of falls 1 (0-20). Outdoors, seven patients (5/2 male/female) had started to use an electric wheelchair or similar, mean (SD) age 47.0 (7.9) years and mean (SD) time since symptom onset 19.6 (11.5) years, at baseline.

3.7 Reported number of falls, injuries and fear of falling

The median number of falls was unchanged (1 and 2 respectively) at the five-year assessment, Table 2, but the number of patients experiencing at least one fall had increased from 58% to 77% p=0.06, not reaching statistical significance. All men had fallen at least once during the year before Y5, which was a significant change from baseline (n=12 (67%) at baseline, n=18 (100%) at

Y5, $p<0.05$), while among the women there was a much lesser, and not significant, increase of whom had fallen at least once (from n=13 (52%) to n=15 (60%). Nearly half of the studied group (n=21, 49%) had fallen three times or more; at baseline this was the case for a third of the group. The proportion of patients reporting injuries needing hospital or primary care after falls had increased significantly from 28% to 53% ($p<0.05$). The injuries varied from bruises and wounds to ankle fractures and head/facial injuries, with seven patients suffering from head/facial injuries two or more times, see Figure 3. At Y5, 63% were afraid of falling compared to 37% at baseline, a statistically significant change ($p<0.01$). Due to fear of falling 60% avoided activities at Y5, versus 42% at baseline, the change did not reach statistical significance. Among the women, 21 reported walking problems at Y5, a worsening from 15 at baseline ($p<0.05$).

4 Discussion

The present study has shown statistically significant decreases over five years in muscle force on all leg muscle groups examined and in all gait and performance-based balance measures in a muscular impaired DM1 cohort. The relative decrease was larger in the distal muscles than in the proximal, which has also been demonstrated in previous reports [7]. The proportion of (male) individuals who had fallen had increased and there was a statistically significant increased fear of falling. These individuals might be considered for a rehabilitation period by a physiotherapist or a more frequent follow-up than the yearly visits by the care provider recommended in the Scandinavian reference programme [30]. However, no studies have been conducted in individuals with DM1 addressing the efficacy of physical training in order to improve postural control or decrease the number of falls. Decline in cognitive functions has been shown to contribute to falls in elderly people [31]. A mild cognitive decline is quite common in patients with DM1 [4], and whether this could contribute to falls should be addressed in future research. Frequent follow-ups with monitoring of function and discussion regarding falls and stressing of the use of walking aids, orthotics and/or wheelchair may reduce the number of falls in individuals with DM1.

4.1 Gender

In women, a statistically significant change after five years was shown in the hip flexors (-1.3%), only. In men, though, there was a significant decrease in all examined muscle groups after five years, with an average yearly decline between -1.5% (hip flexors) and -4.5% (ankle dorsiflexors). At the five-year assessment all men (100%) reported that they had fallen the previous year. Taken together, this could be an indication of worse disease progression in men. The baseline data in the mapping study showed a larger muscular impairment in the men, although the mean age was the same in both men and women. One finding was that the ankle dorsiflexor force was greater at baseline for women than for men, however, the decrease for men was considerably larger than for women, both in absolute and relative figures. Statistically significant differences between changes in males vs. females were shown however only in knee extensors and flexors, $p < 0.05$ in both. Future studies of sex differences need a larger participant number to be evaluated without the risk of type II error. Consequently, it could be of importance to be aware of these possible differences in future research, when including individuals in clinical studies with various therapies in DM1.

4.2 Timed 10-m walk, TUG and Step test

We found a statistically significant decrease in the timed walk and the performance-based measures of balance after five years, both in the whole group and for men and women respectively. The first moments of timed walking and the Step test were very difficult for some individuals, as they had great difficulty in standing still in the initial part of the tests, which is a sign of impaired postural control. Another sign of impaired postural control was inability to complete the Step test during the 15 seconds. The TUG test includes rising and sitting down which are more dependent on force in the proximal muscle groups of the lower extremities. The included turning could be a challenge for the postural control. Altogether, it seems important to use several tests to capture different aspects of impairments in postural control.

4.3 Reported balance confidence and falls

After five years the balance confidence had decreased 10 points or more in 17 individuals. A change of this degree infers an augmented risk of falling with about 49% [12]. What we found was an increase in the number of individuals experiencing a fall and, more importantly, an increase in the need for medical care as a consequence of the falls. While the number of falls was unchanged, falls leading to reported bodily injuries, including several head and facial injuries as well as ankle fractures, increased. The occurrence of head and facial injuries may be explained by the insufficient protective function due to upper extremity weakness [14]. The risk of injuries when a fall occurs in an individual with DM1 is therefore obvious. Not surprisingly, the number of individuals avoiding activities due to fear of falling had increased, as had the number of individuals reporting that they were afraid of falling.

4.4 Study limitations

The study design narrowed the inclusion criteria to a muscular impaired DM1 group, with exception for those with a large impairment at baseline. Hence, the results are only generalizable to muscular impaired individuals with DM1. The retrospective reporting of falls could make the reporting less trustworthy, a recall bias, as the data are supported only by memory. The semi-structured questions on the fall incidents helped the individuals to remember the specific falls and the related trauma, which aimed to contribute to the reliability. Only muscle groups amenable to handheld dynamometry were assessed. This excluded potentially important muscle groups for walking, sit to stand and balance, namely hip extensors and plantar flexors. These muscle groups could be worth considering in future studies. The study was performed with the eligible patients with DM1 in the western part of Sweden, and no power estimation has been done. For further subgroup analysis a larger study sample would be recommended.

4.5 Conclusions

We have studied a DM1 cohort during a five-year period. We could show that the falls, although they did not increase in numbers, included a larger proportion of the individuals. These individuals encountered more severe injuries, which led to a higher degree of need for medical care services. Both males and females showed significant changes in the dynamic balance tests, but the deterioration in muscle force showed to be more severe in males. We find it imperative to follow this patient group continuously, ask them about falls and refer them to physiotherapy treatment and follow-up. Further studies are requested to evaluate if rehabilitation interventions, including alternative balance strategies, in the long-term care of individuals with DM1 could lead to a diminished rate of falls in the future.

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Table 1. Characteristics at baseline of patients with DM1 included in final analysis; in total and by gender; and also of early dropouts from the original 46 patients.

	In final analysis included patients, n=43				**Dropouts, n=3**
	All N=43	Men N=18	Women N=25	Difference between men/women P value	Gender N=3 1 male, 2 females
CTG	558 (385) *475(64-2000)*	580 (253) *590(105-1100)*	543 (461) *450(64-2000)*	0.29	607 (346) *470(350-1000)*
Age	41.0 (9.1) *39 (23;60)*	40.8 (9.8) *40.5 (23;60)*	41.1 (8.7) *39 (25;58)*	0.93	45 (2.6) *46 (42-47)*
Disease duration	14.3 (9.0) *11 (1-40)*	13.8 (5.9) *11 (4-25)*	14.7 (10.7) *10 (1-40)*	0.72	22.3 (11.6) *28 (9-30)*
DEX, N	130 (86) *111 (5-450)*	101 (102) *71.5 (5-450)*	151 (66) *176 (30-246)*	0.006	71 (16) *64 (59-89)*
ABC score	71 (24) *77 (21-99)*	64 (27) *65 (21-99)*	75 (20) *81 (38-98)*	0.28	54.6 (22.5) *65 (29-70)*
MIRS 1	0 (0%)	0 (0%)	0 (0%)		-
2	0 (0%)	0 (0%)	0 (0%)		-
3	16 (37%)	2 (11%)	14 (56%)	0.001	-
4	24 (56%)	13 (72%)	11 (44%)		3 (100%)
5	3 (7%)	3 (17%)	0 (0%)		-

Abbreviations: CTG, CTG-repeats; DEX, ankle dorsiflexor force, in newton; ABC, activities-specific balance confidence; MIRS, muscular impairment rating scale.

Table 1, legend: Age and disease duration (time since symptom onset) are presented in years. For continuous variables mean (SD) and *median (min; max)* are presented. MIRS grade distribution is presented in number and percentage. For comparison between two groups (genders) Mann Whitney U test was used for continuous variables, and Mantel-Haenszel Chi Square Exact test for ordered categorical variables (MIRS).

Table 2. Results of the measurements at baseline and after five years (Y5), in total; and change from baseline to Y5 in total and by gender.

	All N=43			**Men** N=18	**Women** N=25	**P value**
	Baseline	**Y5**	**Change[a]**	**Change[a]**	**Change[a]**	**Comp between genders[b]**
Hip flexors, (N)	171 (39) *172(114;283)*	159 (36) *155(86;232)*	-12 (18) *-12(-57;26)****	-14 (25) *-14.8(-57;26) **	-10.7 (13) *-12(-38;19) ****	*0.67*
Knee extensors, (N)	274 (95) *274(92;474)*	258 (103) *269(47;473)*	-15 (43) *-17(-98;105)**	-35 (33) *-37(-95;30) ****	-1.7 (45) *-2.7(-98;105)*	*0.019*
Knee flexors, (N)	101 (33) *106(3.5;171)*	93 (35) *101(0;154)*	-8.0 (14) *-8.2(-38;23)***	-13.2 (14.3) *-16.3(-38; 23) ***	-4.2 (12) *-0.5(-28;19)*	*0.021*
Ankle dorsiflex, (N)	130 (86) *111(5;450)*	115 (91) *74(3;395)*	-15 (30) *-10(-93;55)***	-22 (26) *-12.4(-93;20)****	-9.8 (33) *-9.2(-88;55)*	*0.20*
10mMAX (seconds)	7.5 (2.4) *7.1(4.6;16.9)*	9.3 (4.3) *8.6(5.1;24)*	1.8 (2.5) *1.1(-1.2;12)****	2.5 (3.2) *1.1(0.1;12.1) ****	1.2 (1.7) *0.9(-1.2;7.3) ****	*0.21*
TUG (seconds)	9.6 (2.4) *9.1(6.5;17.5)*	12.0 (5.4) *10.4(7;34)*	2.3 (4.1) *1.6(-3.4;19)****	3.0 (4.8) *2.0(-3.1;19.3) ***	1.9 (3.5) *1.5(-3.4;16.9) ****	*0.42*
STEP (steps)	13.3 (5.4) *13(0;23)*	10.7 (6.5) *11.5(0;22)*	-2.5 (3.7) *-1.5(-10.5;4)****	-2.4 (3.8) *-1.7(-9;4) **	-2.6 (3.8) *-1.5(-10.5;4) ***	*0.91*
ABC score	71 (23) *77(21;99)*	64 (25) *67(13;99)*	-7 (18) *-5(-49;32)**	-10 (19) *-10(-38;32) **	-4 (17) *-3(-49;26)*	*0.17*
Number of falls	4.7 (10.4) *1(0; 60)*	3.8 (4.4) *2(0; 20)*	-0.9 (10.3) *0(-50;19)*	2.0 (5.4) *1 (-8; 19)*	-3 (12.4) *0(-50;11)*	*0.13*

Abbreviations: Y5, at assessment after five years; Comp, comparison of changes; N, newton; 10mMAX, time to walk 10 meter; TUG, Timed Up & Go; STEP, number of steps in Step test; ABC, activities-specific balance confidence scale.

Table 2 legend: For continuous variables mean (SD) and *median(min; max)* are presented. For the categorical variables n (%) are presented. Due to lack of space the probability is marked by signs: * = p<0.05, ** = p< 0.01, ***p<0.001.

[a] For comparison within individuals the Wilcoxon Signed Rank test was used for continuous variables and Sign test was used for categorical variables.

[b] For comparison of change between genders Mann-Whitney U test was used for continuous variables and the Mantel-Haenszel Chi Square Exact test was used for ordered categorical variables.

Table 3. Results of correlation analysis between absolute changes in dynamic tests (baseline to assessment year 5) and relative changes in muscle force (difference /baseline force, in percent). N=43.

	Spearman's rho					
	10mMAX **Δ**		TUG **Δ**		STEP **Δ**	
	Rho	P value	Rho	P value	Rho	P value
Hip flexors **Δ** %	-0.23	0.14	-0.26	0.10	0.07	0.67
Knee extensors **Δ** %	-0.61	<0.001	-0.64	<0.001	0.47	0.002
Knee flexors **Δ** %	-0.46	0.002	-0.46	0.002	0.33	0.031
Ankle dorsiflexors **Δ** %	-0.50	0.001	-0.50	0.001	0.47	0.002

Abbreviations: 10mMAX, time to walk 10 meter; **Δ**, difference; TUG, Timed Up & Go; STEP, Step test.

Table 3. Legend: The relative changes in muscle force were in all leg muscles but the hip flexors moderately correlated to the absolute changes in dynamic balance. The strongest (negative) correlations were shown for TUG and 10mMAX to the change in knee extensors. The Step test was shown to be moderately positively correlated to the knee extensors and the ankle dorsiflexors.

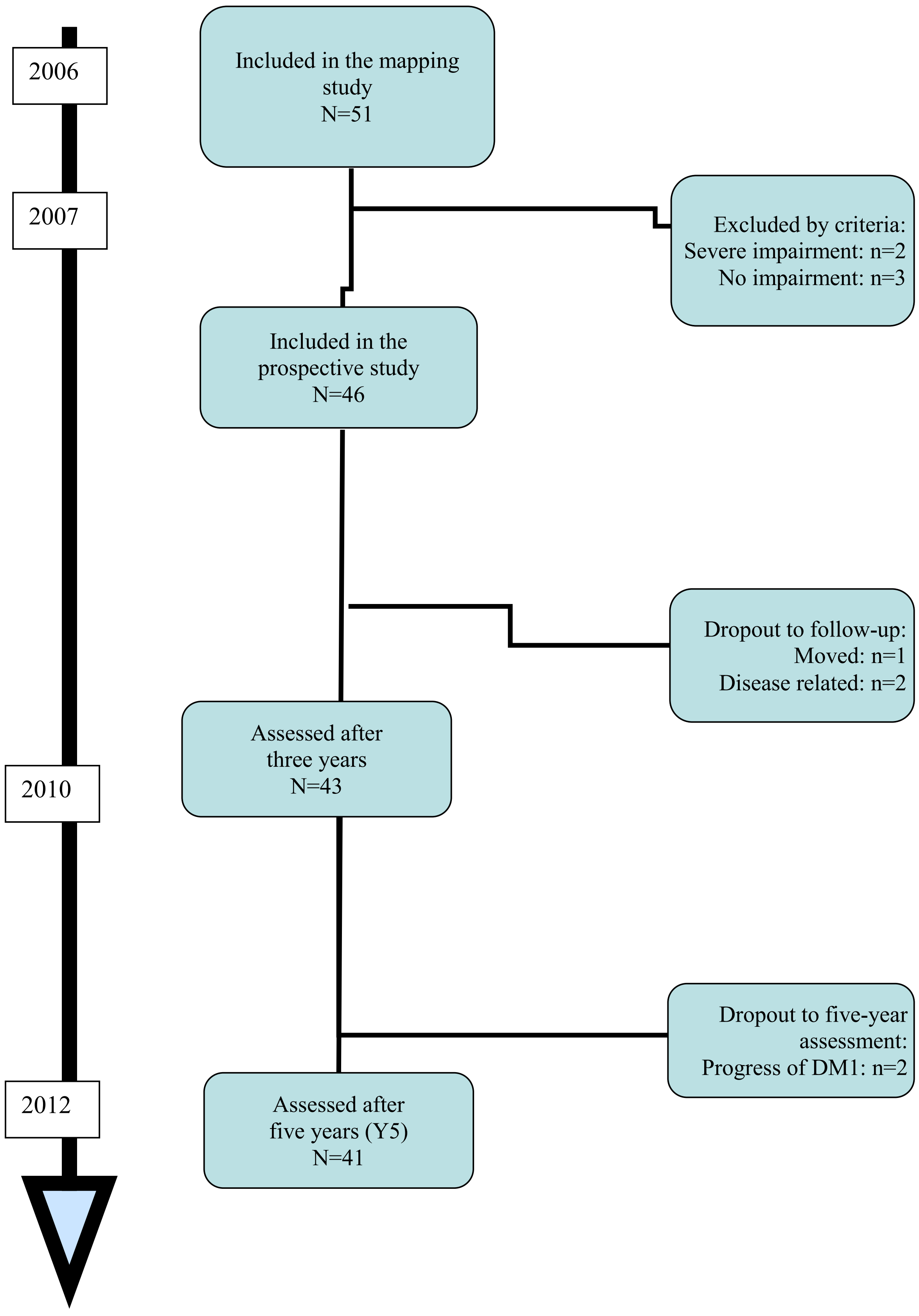

Figure 1. Flowchart

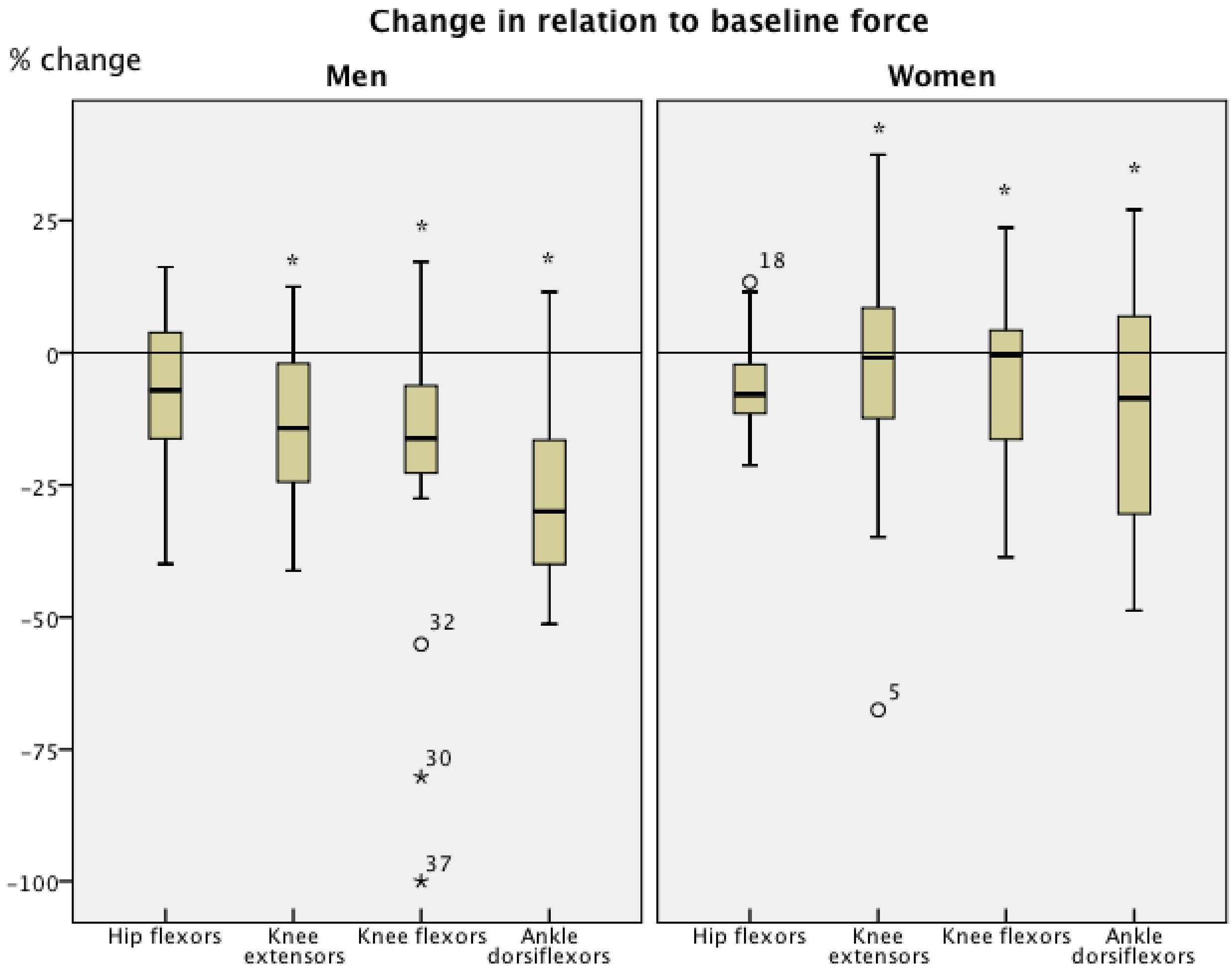

Figure 2. Boxplot of relative changes in muscle force after five years for men (N=18) and women (N=25) in percent of baseline force.

Figure 2 legend: Each box includes 50% of the group, the top and bottom line represents the first and third quartiles, the line inside the box shows median and the whiskers show min-max within interquartile range. Outside values are marked with a circle and far outside values are marked with asterisks, both with ID number. A reference line is included at zero change. A worse result is going beneath the reference line. The null hypothesis is tested with non-parametric statistics, Mann-Whitney U test. A significant difference ($p<0.05$) between genders in relative change is marked with an asterisk above the box of each muscle group.

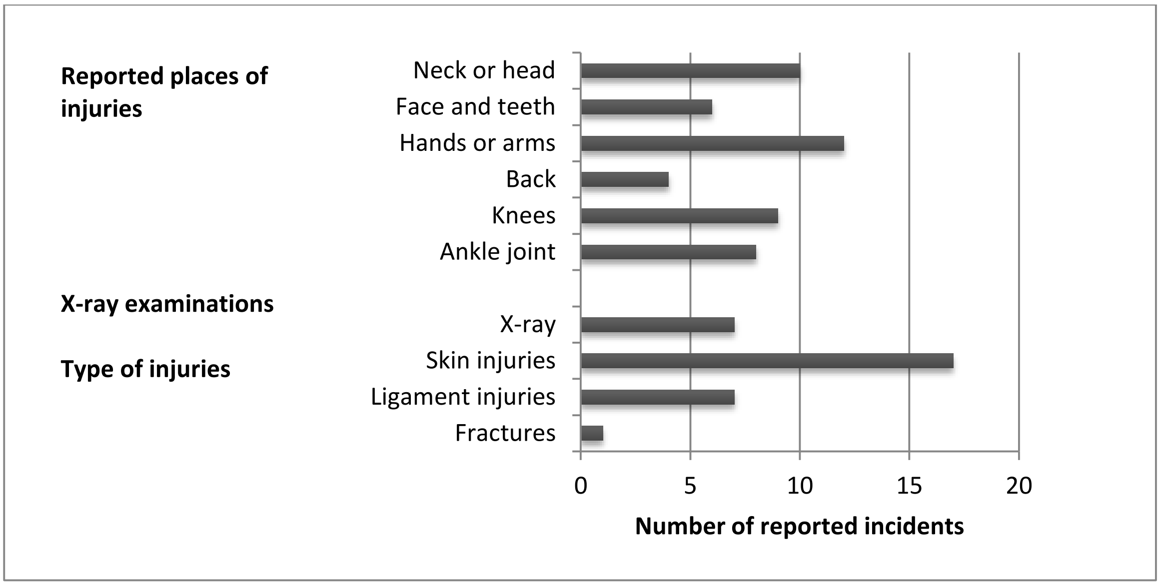

Figure 3. Reported injury frequencies, x-ray examinations and injury types.