HIP STRENGTH: ANKLE PROPRIOCEPTIVE THRESHOLD RATIO PREDICTS FALLS AND INJURY IN DIABETIC NEUROPATHY

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ABSTRACT: Introduction: We determined lower limb neuromuscular capacities associated with falls and fall-related injuries in older people with declining peripheral nerve function. Methods: Thirty-two subjects (67.4 \pm 13.4 years; 19 with type 2 diabetes), representing a spectrum of peripheral neurologic function, were evaluated with frontal plane proprioceptive thresholds at the ankle, frontal plane motor function at the ankle and hip, and prospective follow-up for 1 year. Results: Falls and fall-related injuries were reported by 20 (62.5%) and 14 (43.8%) subjects, respectively. The ratio of hip adductor rate of torque development to ankle proprioceptive threshold (HipSTR/Ank_PRO) predicted falls (pseudo-R² = .726) and injury (pseudo-R² = .382). No other variable maintained significance in the presence of HipSTR/Ank_PRO. Conclusions: Fall and injury risk in the population studied is related inversely to HipSTR/Ank_PRO. Increasing rapidly available hip strength in patients with neuropathic ankle sensory impairment may decrease risk of falls and related injuries.

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Distal symmetric polyneuropathy (DSP) is common in older patients with type 2 diabetes mellitus (DM); it occurs in approximately 30% of those between ages 70 and 80 years. Furthermore, older people without DM may have subclinical declining peripheral nerve function (DPNF) that does not fully meet criteria for a DSP. Precise epidemiologic data are unavailable, but the prevalence is sufficient that age-related adjustments in peripheral nerve function have been made for physical examination, nerve conduction studies, and unipedal stance time. 5,6

The laudatory health benefits of walking include reductions in mortality in men,⁷ reductions in cognitive decline in women,⁸ and reductions in new cases of obesity and type 2 DM,⁹ along with improved metabolic control and decreased total mortality in those already with the disease.^{10,11} However, walking for exercise often leads to falls^{12–14} and curtailment of activity,¹⁵ with resultant deleterious effects on metabolic parame-

Abbreviations: AnkPRO, ankle proprioceptive threshold; cm, centimeter; DPNF, declining peripheral nerve function; DM, diabetes mellitus; DSP, distal symmetric polyneuropathy; Hz, Hertz; Hip^{STR}, hip strength; HipSTR/AnkPRO, ratio of hip strength to ankle proprioceptive threshold; MVS, maximum voluntary strength; MDNS, Michigan Diabetes Neuropathy Score; ms, millisecond; mV, millivolt; Nm, Newton-meter; RTD, rate of torque development

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ters¹⁰ and vascular risk factors.¹⁶ Moreover, fall risk is increased markedly in those with DSP^{17,18} and in patients with age-related DPNF who demonstrate intrinsic foot muscle atrophy,¹⁹ increased ankle proprioceptive thresholds,²⁰ and reduced lower limb strength, physical performance, and mobility.^{21–23} Collectively, these studies suggest that peripheral nerve dysfunction contributes to agerelated mobility loss and susceptibility to accidental falls.

Although prior work confirms the deleterious

Although prior work confirms the deleterious influence of peripheral nerve impairment on quantified measures of ankle sensory 24,25 and motor function, 26,27 the precise lower limb neuromuscular function(s) responsible for this susceptibility are not known. To address this, we recently evaluated ankle proprioceptive thresholds (Ank-PRO), as well as ankle and hip strength (Hip^{STR}), in 41 older subjects with a spectrum of peripheral neurologic function. Neuromuscular capacities were studied in the frontal plane (i.e., ankle inversion/eversion and hip ab/adduction), because impairment in lateral (frontal plane) control increases fall risk $^{29-31}$ and the injury potential of laterally directed falls. The results showed that unipedal stance time was predicted by the ratio of Hip^{STR} to Ank_{PRO} (Hip^{STR}/Ank_{PRO}; $R^2 = .75$). The results are supplied to the ratio of Hip^{STR} to Ank_{PRO} (Hip^{STR}/Ank_{PRO}; $R^2 = .75$).

Therefore, we hypothesized that Hip^{STR}/Ank-PRO would also be responsible for susceptibility to falls and fall-related injuries in the community. To test this, we studied a subset of the same subjects for 1 year by prospectively recording falls and fall-related injuries. We hypothesized that subjects with decreased Hip^{STR}/Ank_{PRO} would be at increased risk for falls (H1) and fall-related injuries (H2).

MATERIALS AND METHODS

Subjects. Forty-one subjects (16 healthy older subjects and 25 subjects with PN due to diabetes) were recruited under a protocol approved by the Institutional Review Board. Written informed consent was obtained from all participants. Nine subjects chose not to participate. Subjects cited personal concerns with their schedules or preference to avoid the associated time commitment as reasons for not participating. Therefore, a subset of subjects (32 subjects, 19 with diabetic DSP and 13 without) agreed to be monitored prospectively

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for 12 months for falls and fall-related injuries using biweekly fall calendars and follow-up telephone calls. Subjects were recruited from the University of Michigan Orthotics and Prosthetics Clinic, Endocrinology Clinic, and the Older Americans Independence Center Human Subjects Core. Inclusion criteria for DSP subjects were as follows: between ages 50 and 85 years; weight <136 kg (due to structural limits of laboratory equipment); known history of diabetes mellitus; able to walk > 30 feet without assistance or assistive device; strength of ankle dorsiflexors, invertors, and evertors at least anti-gravity (grade ≥3/5 by manual muscle testing); symptoms consistent with DSP(symmetrically altered sensation in lower extremities); signs consistent with DSP (Michigan Diabetes Neuropathy Score; MDNS ≥10);³⁴ Electrodiagnostic evidence of DSP as evidenced by bilaterally abnormal fibular motor nerve conduction studies (absent or amplitude <2 mV and/or latency >6.2 ms and/or conduction velocity <41.0 m/s) stimulating 9 centimeters from recording site over the extensor digitorum brevis distally and distal to fibular head proximally.

Exclusion criteria for DSP subjects included accidental fall 1 month or less before testing, evidence of central nervous system dysfunction, neuromuscular disorder other than DSP, vestibular dysfunction, functionally-limiting angina, plantar skin sore, joint replacement within the year before testing, symptomatic postural hypotension, musculoskeletal deformity (e.g., Charcot changes or any amputation), lower limb or spinal arthritis, or pain of any kind that limited standing to < 10 min and/or walking to less <1 block.

The healthy older adults met the same inclusion and exclusion criteria as the DSP subjects but were without neuropathic symptoms, had an MDNS score <10, and normal bilateral fibular motor nerve conduction studies recording at the extensor digitorum brevis.

Entrance Evaluation. The initial evaluation included a history and physical examination to evaluate for inclusion criteria and exclusion criteria. Neuropathy severity was determined further using the 46 point scale MDNS (with higher scores reflecting increasingly severe DSP) which evaluates distal sensory and motor function and muscle stretch reflexes.³⁴ Finally, all subjects underwent bilateral nerve conduction studies of the fibular nerve, as described above.

Laboratory Measures of Lower Limb Neuromuscular Capacities (Independent Variables for H1 and H2). Each of the techniques for measuring frontal plane lower limb sensorimotor function have been described in prior work. 24,28,35

Hip abduction and adduction strength evaluation (Hip^{STR}). Maximum voluntary strength (MVS) and rate of torque development (RTD) of the frontal plane hip muscles were measured using a custom designed, whole-body dynamometer (Bio Logic Engineering, Inc., Dexter, Michigan).^{28,35} The dynamometer has a horizontal bench on which the subject lies, allowing measurements to be made in a gravity-free plane. The pelvis and trunk were immobilized using harness straps at multiple points. During abduction MVS testing, subjects progressively increased their isometric effort from rest to maximum over a count of 3, then held it for 2 s, and relaxed. Subjects were encouraged verbally. To quantify RTD, subjects abducted the lower limb against the lever arm "as quickly and as hard as possible" for 3 s. Subjects performed 3 trials with 1 min rest between each trial. Subjects performed analogous maneuvers in the opposite direction for hip adduction MVS and RTD testing.

Ankle Inversion and Eversion Strength Evaluation. To measure ankle inversion/eversion MVS and RTD, 28,35 subjects stood on the test foot on a 6-axis force plate (Model OR-6, AMTI, Watertown, Massachusetts). After being familiarized with the procedure, RTD was determined by subjects moving the center of ground reaction from the lateral margin of the foot (inversion) to the medial margin (eversion) as quickly as possible, then again quickly to the lateral margin, and then repeated the sequence 5 times. Three trials were performed. Subjects were allowed to touch a nearby horizontal railing to maintain balance.

For determination of MVS, subjects again stood on the force platform, touching the hand rails on both sides as needed. Subjects lifted 1 leg, shifted their center of gravity as far lateral (inversion) under the foot as possible, and lifted their hands from the rails for 3 s. The test was repeated 3 times for the lateral, and then likewise repeated for the medial margin (eversion) of the foot.

Ankle Inversion/Eversion Proprioception Thresholds (Ank_{PRO}). Subjects stood with the test foot in a 40 \times 25 cm cradle that was rotated by an Aerotech 1000 servomotor equipped with an 8,000 line rotary encoder. A single ankle inversion or eversion rotation of 0.1 to 3° magnitude was presented randomly at 5°/s after a discrete audible cue. In response, the subject rotated a joystick handle in the direction of the perceived foot rotation. Four blocks of 25 trials (randomly 10 eversion, 10 inversion, and 5 dummy trials) were presented, with 2-to 5-min rest intervals between blocks. Subjects were instructed not to guess the direction, and the dummy trials provided a check on guessing behavior. Ank_{PRO} was defined as the smallest rotational

Table 1. Subject characteristics.			
	Overall N = 32	(+) Diabetes mellitus* N = 19	(-) Diabetes mellitus* N = 13
Age (years)	68.5 ± 8.2	69.7 ± 8.8	66.8 ± 7.1
Gender (% Women)	15 (46.9)	7 (36.8)	8 (61.5)
Body Mass Index	30.5 ± 6.6	32.6 ± 5.5	27.2 ± 6.9
MDNS score	8.3 ± 7.8	13.6 ± 5.5	0.6 ± 1.1

^{*(+)} Denotes the presence of diabetes mellitus, and (-) denotes its absence.

ankle displacement that a subject could detect with 100% accuracy. 24

Data Processing. Signals were amplified to volt levels before being acquired using a 12 bit analogto-digital converter sampling at 100 Hz. The MVC efforts at the hip and ankle and the maximal RTD were normalized by individual body size defined as the parameter body height multiplied by weight in units of Nm. Strength data were processed using a Labview second-order least squares polynomial fit to determine the peak value. The mean peak value obtained from the 3 trials for each test type was used for the statistical analyses. To determine each proprioceptive threshold, the mean TH₁₀₀ from the 4 blocks of 25 trials in each test direction was calculated. A summary measure of ankle proprioception was found from the sum of the inversion and eversion proprioception threshold.

Recording Falls (Dependent Variable H1). Falls were recorded using methods described by Tinetti et al.³⁶ Each subject was given 26 calendars, each of which recorded a 2-week span. Each day the subject checked a box to indicate if he/she had experienced a fall, and to comment on its nature and circumstances. At the end of each 2-week period, subjects returned the surveys by mail. If no response was received 2 weeks after the calendar due date, or if a fall was indicated, the research coordinator contacted the subject. A fall was defined as an unintentional change in body posture that results in the subject coming to rest on the ground or other lower level that was not a consequence of a physical blow or loss of consciousness. No predetermined threshold for exclusion due to calendar return noncompliance was established. On the rare occasions a subject did not return a calendar, the study coordinator was able to communicate with the subject within 5 days to determine the presence of a fall or fall-related injury during the missed interval.

Recording Fall-Related Injury (Dependent Variable H2). Fall-related injuries were also recorded as per Tinetti et al.³⁶ Fall-related injuries were classified as major and minor, with the former meeting crite-

Table 2. Clinical variables in subjects categorized by fall status.

	$(-)$ Fall $(n = 12)^*$	$(+)$ Fall $(n = 20)^*$	P value
Age	64.5 ± 6.8	70.9 ± 8.2	0.030
Gender (n/% women)	5 (41.7%)	10 (50%)	0.647
BMI	28.2 ± 7.6	31.7 ± 5.7	0.147
MDNS	1.3 ± 2.6	12.5 ± 6.8	< 0.001

^{*(-)} Denotes absence of a fall, and (+) denotes the presence of a fall.

ria for an Abbreviated Injury Scale Score > 2, ³⁷ and the latter including all other injuries such as bruises, abrasions, and lacerations not requiring sutures that prevented or changed the way a subject performed a basic ADL for at least 24 h. ³⁸

Statistical Analyses. Fall and fall-related injury group differences in mean lower limb neuromuscular capacities were evaluated using standard *t*-tests. Continuous demographic and clinical variables (age, MDNS score, body mass index) were also evaluated by *t*-test, while gender was evaluated by chi-square analysis. Binary logistic regression was used to determine which laboratory-based measures of lower limb neuromuscular function were the strongest independent predictors of falls and fall-related injury, with variables demonstrating the strongest univariate relationships entered into the model first. Clinical/demographic variables were added as appropriate, again based on strength of univariate analyses.

RESULTS

Subjects. Subject characteristics are provided in Table 1.

Fallers vs. Non-Fallers (H1). After 1 year of prospective follow-up, 20 of the 32 subjects (62.5%) reported 1 or more falls. These subjects were significantly older and had significantly higher MDNS scores, indicating more severe DSP (Table 2). There were significant fall group differences in all lower limb neuromuscular capacities except for

Table 3. Laboratory measures of lower limb neuromuscular capacities in subjects categorized by fall status.

	$(-)$ Fall $(n = 12)^*$	$(+)$ Fall $(n = 20)^*$	P value
Hip Abd MVS	.46 ± .25	.32 ± .10	0.029
Hip Abd RTD	$.31 \pm .18$	$.14 \pm .09$	0.001
Hip Add MVS	$.50 \pm .19$	$.34 \pm .13$	0.012
Hip Add RTD	$.40 \pm .20$	$.16 \pm .15$	< 0.001
Ank _{PRO}	0.8 ± 0.3	2.3 ± 1.4	0.001
Ankle Inv MVS	$2.1 \pm .6$	$1.5 \pm .6$	0.035
Ankle Inv RTD	.21 ±. 10	$.10 \pm .07$	0.003
Ankle Ev MVS	$1.0 \pm .3$	$1.4 \pm .7$	0.076
Ankle Ev RTD	$.25 \pm .13$	$.13 \pm .07$	0.005
Hip ^{STR} /Ank _{PRO}	$.61 \pm .39$	$.10 \pm .11$	< 0.001

 $^{^{\}star}(-)$ Denotes absence of a fall, and (+) denotes the presence of a fall.

Table 4. Clinical/demographic variables categorized by fall-related injury status.

	(-) Injury $(n = 18)^*$	(+) Injury $(n = 14)^*$	P value
Age	66.1 ± 6.9	71.6 ± 8.9	0.060
Gender	7 (39%)	8 (57%)	0.305
BMI	29.7 ± 7.6	31.3 ± 5.1	0.515
MDNS	5.5 ± 7.0	11.9 ± 7.4	0.018

^{*(-)} Denotes absence of a fall-related injury, and (+) denotes its presence

ankle eversion MVS, with fallers demonstrating decreased strength measures and increased (less precise) ankle proprioceptive thresholds (Table 3). The greatest group differences for individual variables were for Hip Adductor and Abductor RTD, and Ank-PRO. Notably, mean Hip STR/Ank_{PRO} (using Hip Adductor RTD for Hip STR) in subjects who fell was approximately one-sixth of that in subjects who did not fall. Multivariate analysis demonstrated that the Hip^{STR}/Ank_{PRO} ratio was the single greatest predictor of falls (pseudo- $R^2 = .726$; P = 0.005). No other demographic or laboratory-based variable, including Hip^{STR} or Ank_{PRO} used singly, or the MDNS measure of neuropathy severity, demonstrated significance in its presence.

Fall Injury versus No Fall Injury (H2). After 1 year of prospective follow-up, 14 of 32 subjects (43.8%) reported a fall-related injury (Table 4). There were significant group differences in Hip Abductor and Adductor RTD, but not in MVS (Table 5). Ank_{PRO} and Ankle Inversion RTD group differences approached significance. Using Hip Add RTD for Hip^{STR}, mean Hip^{STR}/Ank_{PRO} in the injured subjects was approximately one-fourth that in the noninjured subjects. Multivariate analysis demonstrated that Hip^{STR}/Ank_{PRO} was the best predictor of fallrelated injury (pseudo- $R^2 = .382$; P = 0.023). As was the case for falls, no other demographic, clinical, or laboratory-based variable demonstrated significance in its presence.

Subgroup Analyses. When subjects with and without diabetes mellitus were evaluated separately, asymmetric fall and fall-related injury group sizes hindered meaningful statistical group comparisons (17 of 19 diabetic subjects reported a fall; 3 of 13 subjects without diabetes reported a fall). However, the data suggest that Hip^{STR}/Ank_{PRO} is decreased in subjects who fall or sustain a fall-related injury. More specifically, in diabetic subjects who reported a fall, Hip^{STR}/Ank_{PRO} was $.083 \pm .097$ versus $.497 \pm .369$ in the 2 subjects with diabetes who did not fall. Similarly, in subjects without diabetes Hip^{STR}/Ank_{PRO} was $.173 \pm .180$ in those who reported a fall and .628 ± .406 in those who did

Comparisons with Other Research. Although differences in subject numbers and techniques prevent perfect comparisons, an evaluation of the relative potency of Hip^{STR}/Ank_{PRO} as compared to other identified potentially modifiable predictors of falls is of interest. To perform these comparisons, Hip^{STR}/Ank_{PRO} was dichotomized after inspecting the data using a cut-off of 0.25, which was near the mean of 0.28. The resulting odds ratios were compared with those from other prospective studies predicting falls. Table 6 suggests that Hip^{STR}/Ank-PRO is a comparatively robust predictor of falls.

DISCUSSION

In this study of older subjects with a spectrum of peripheral neurologic function due to age and diabetes mellitus, the ratio of rapidly generated frontal plane hip strength to frontal plane ankle proprioceptive threshold (Hip^{STR}/Ank_{PRO}) was the best and only significant predictor of prospectively determined falls (H1) and fall-related injuries (H2). This novel measure of lower limb neuromuscular function was responsible for more than 70% of fall likelihood and nearly 40% of fall-related injury likelihood. The results are unique in 2 respects. Although other research has measured ankle proprioceptive thresholds (in the sagittal plane) in diabetic subjects²⁵ and hip strength in older subjects, ^{39,40} no prior research has obtained them within the same subjects. Accordingly, the main finding that the ratio of proximal strength to distal proprioceptive precision predicts falls and fall-related injury in the community is novel. Secondly, we could not identify any other study which used laboratory-based measures of lower limb function to predict fall-related injury.

The impact of increased ankle proprioceptive thresholds on balance has been described,²⁴ and the importance of frontal plane hip strength to dynamic lateral balance emphasized. 41 However, the relevance of the ratio of hip strength to ankle proprioceptive precision with regard to rejecting a

Table 5. Laboratory measures of lower limb neuromuscular capacities in subjects categorized by fall-related injury status.

	(-) Injury $(n = 18)^*$	(+) Injury (n = 14)*	P value
Hip Abd MVS	.40 ± .22	.32 ± .11	0.191
Hip Abd RTD	$.26 \pm .18$	$.13 \pm .07$	0.013
Hip Add MVS	$.43 \pm .02$	$.36 \pm .13$	0.252
Hip Add RTD	.33 + .22	.15 + .12	0.009
Ank _{PRO}	1.3 ± 1.0	2.2 ± 1.5	0.058
Ankle Inv MVS	$1.8 \pm .7$	$1.5 \pm .6$	0.328
Ankle Inv RTD	$.17 \pm .11$	$.10 \pm .07$	0.056
Ankle Ev MVS	$1.2 \pm .6$	$1.0 \pm .3$	0.238
Ankle Ev RTD	$.20 \pm .12$	$.134 \pm .08$	0.105
Hip ^{STR} /Ank _{PRO}	$.43 \pm .40$	$.10 \pm .12$	0.006

^{*(-)} Denotes absence of a fall-related injury, and (+) denotes its presence.

Table 6. Comparison of Hip^{STR}/Ank_{PRO} as a predictor of falls Strongest modifiable Data source predictor of falls Odds ratio, (95% CI) Hip^{STR}/Ank_{PRO} 28.6 (4.1-200) Present study Delbaere et al.47 Vision/knee strength 1.30 (1.02-1.67) Leveille et al.48 Severe pain 1.77 (1.32-2.38) Lord et al.49 Vision 2.29 (1.06-4.92) Stel et al.50 Lateral sway 2.8 (1.1-6.9) Hausdorff et al.51 Gait variability 5.3 (1.01-27.2) Hilliard et al.52 >1 Step with 6.16 (1.74-21.8) perturbation

perturbation while walking is less obvious and deserves comment. A useful model of human balance is that of an inverted pendulum (for example, Loram and Lakie, 2002). 42 Increased rate of torque development allows rapid development of a co-contraction about the hip in response to a perturbation so as to quickly stiffen the joint, which then "lengthens" the pendulum so as to slow the rate of descent of the perturbed body. This increases the time available for a rescue strategy, such as placement of the swing limb medially or laterally to arrest lateral momentum. This rationale is consistent with the finding that type II fiber atrophy of the gluteus medius is an independent fall risk factor. 43 Rapidly available torque at the hip would also allow the swing limb to be moved quickly into position to arrest momentum after a perturbation is perceived.44 Precise ankle proprioceptive thresholds allow earlier perception of a perturbation, a situation in which less time, and therefore less hip strength, would be necessary for either stabilization or swing limb positioning. The predictive strength of the ratio, being greater than either variable in isolation, suggests that an older person can tolerate some degree of increased ankle proprioceptive thresholds if sufficient hip rate of strength generation is available and can withstand some degree of hip weakness if ankle proprioception is sufficiently precise. However, if the hips are weak and proprioceptive thresholds are imprecise, then the ability to withstand a perturbation is reduced, and fall risk increases.

Given that the laboratory-based measures described here require dedicated hardware/software and 90 to 120 min of testing time per patient/subject, direct application to the clinic is not feasible. Despite this, the work has clinical relevance in that Ank_{PRO} can be estimated by means of routine fibular motor compound muscle action potential amplitudes. Neuropathic and older patients with decreased amplitudes are likely to have imprecise ankle proprioceptive thresholds. Due to our present inability to reverse diabetic and age-related neuropathy Hip^{STR}/Ank_{PRO} can only be augmented, and presumably fall and fall-related injury risk reduced,

by increasing hip strength. Therefore, the data suggest that older patients with worsening peripheral nerve function should strive to increase the ability to quickly generate force at the hips, particularly adductor force, a muscle group rarely targeted in fall prevention programs. Other work suggests that this population responds to resistance training. However, if this is not possible and Hip^{STR}/Ank_{PRO} is presumed to be low, then compensatory strategies should be considered. ⁴⁶

The study has strengths and limitations. Among the former, peripheral nerve function was evaluated clinically and electrodiagnostically so that erroneous evaluation of peripheral nerve function is unlikely. The laboratory-based quantification of multiple lower limb sensory and motor capacities within each subject was novel and allowed comparison of the relative importance of these capacities, as well as evaluation of interplay between afferent and efferent lower limb functions. Falls and fall-related injuries were recorded prospectively using recommended techniques. 36-38 The results were robust, with mean Hip^{STR}/Ank_{PRO} being approximately 6 times greater in those who avoided a fall and 4 times greater in those who avoided a fall-related injury; this appeared to apply to the subjects with and without diabetes mellitus. When Hip^{STR}/Ank_{PRO} was evaluated as a dichotomous variable, the resulting odds ratios were also robust in comparison with a sample of published prospective studies identified in the literature for the same outcome (Table 6). Because each subject underwent approximately 10 hours of evaluation before prospective fall and fall-related injury data collection, the number of subjects is relatively small and bias due to sampling error is possible. Additionally, the technique for evaluating ankle inversion/eversion strength while weight-bearing may also include some forces generated by the hip. This may have reduced the influence of ankle strength on the outcomes. Fall-related injuries were by subject report; the absence of objective physical examination could lead to inaccuracy for this outcome. Finally, no data were generated for lower limb functions in the sagittal or transverse planes.

In conclusion, the data suggest that the ratio of hip adductor rate of torque generation to ankle proprioceptive precision is the best predictor of falls and fall-related injuries in older subjects with a spectrum of peripheral neurologic function. Patients with distal afferent impairments in ankle sensory function may benefit from training which emphasizes the ability to rapidly develop muscle strength at the hip, particularly adductor strength. These findings are novel and encourage strengthening of a muscle group that is rarely targeted in fall prevention programs.

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