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Common Carotid Artery Intima-Media Thickness, Carotid Plaques, and Walking Speed

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Background and Purpose**—**Gait dysfunction is an important cause of disability among the elderly and may be, in part, of vascular origin. We studied the association between carotid ultrasound parameters and measures of gait and balance in subjects 65 to 85 years of age who participated in the baseline phase of the Three-City Study in the Dijon center.

Methods**—**The study population comprised 2572 noninstitutionalized individuals. Carotid plaques and common carotid artery intima-media thickness (CCA-IMT) were measured using ultrasonography. Gait and balance measures included walking speed and a modified version of the Tinetti scale.

Results**—**Mean maximum walking speed (MWS) decreased with increasing CCA-IMT and number of plaques ($P<10^{-4}$). Compared with subjects in the lowest CCA-IMT quintile, the odds ratio (95% CI) for being in the lowest MWS quartile was 1.1 (0.8 to 1.6) in the second, 1.3 (0.9 to 1.8) in the third, 1.7 (1.2 to 2.4) in the fourth, and 2.2 (1.6 to 3.1) in the higher CCA-IMT quintile ($P<10^{-4}$). Mean (SD) CCA-IMT was 0.716 (0.118) mm in subjects with a modified Tinetti score <16 (25th percentile) and 0.685 (0.109) mm in subjects with a score of ≥16 ($P=0.006$). The proportion of subjects in the lowest MWS quartile ($P=0.006$) or with a modified Tinetti score <16 ($P=0.05$) increased with the number of plaques. These relations were attenuated after adjustment for vascular risk factors.

Conclusions**—**Carotid plaques and higher CCA-IMT values are associated with worse performances on gait and balance tests. Our results suggest that vascular factors may play an important and under-recognized role in motor function. **(*Stroke*. 2005;36:2198-2202.)**

Key Words: epidemiology ■ gait ■ intima-media thickness ■ motor activity ■ ultrasonography

Gait dysfunction is a frequent cause of disability among the elderly.[1] It increases the risk of falls, functional decline, and death.[1–3] Cerebral multi-infarct states can lead to variously labeled gait disorders (eg, vascular parkinsonism, frontal gait disorder, and "marche à petits pas"),[4] but the contribution of vascular risk factors to the etiology of age-related gait changes (eg, in speed) has received less attention.

Carotid plaques and common carotid artery intima-media thickness (CCA-IMT) are markers of arterial wall alteration. CCA-IMT can be assessed by B-mode ultrasound in a simple way and represents a precise and reproducible measure.[5] CCA-IMT has been associated with most traditional vascular risk factors and is considered to be a cumulative measure of long-term exposure to them.[5,6] In addition, CCA-IMT predicts carotid atherosclerotic plaques and vascular risk[7–9] and has recently been used as the main outcome in clinical trials.[10]

We hypothesized that vascular risk factors may contribute to impair motor function in the elderly. We used carotid plaques and CCA-IMT as surrogates for vascular risk factors and studied their cross-sectional relationship with gait and balance measures as part of the baseline phase of the Three-City (3C) Study in Dijon (France).[11]

Subjects and Methods

The study protocol has been described previously.[11] The 3C Study is a cohort study conducted in 3 French cities (Bordeaux, Dijon, and Montpellier). Noninstitutionalized individuals ≥65 years of age were selected from electoral rolls. The cohort was recruited between March 1999 and March 2001. The acceptance rate was 37%. In addition to the main objective of the study (to estimate the risk of cognitive impairment attributable to vascular risk factors), Dijon investigators were interested in the role of vascular risk factors in motor function. The study protocol was approved by the ethical committee of Kremlin-Bicêtre University Hospital, and all participants signed an informed consent. The study questionnaire is available from the investigators on request or from the study website (http://www.3c-study.com).

Medical Data Collection, Gait, and Balance Tests

Demographic and medical data were collected at home during a face-to-face interview by trained psychologists. Participants aged ≤85 had a subsequent clinical examination at the Dijon study center during which walking speed was measured.[12] Two photoelectric cells connected to a chronometer were placed in a corridor 6 m apart.

Received December 15, 2004; final revision received July 11, 2005; accepted July 21, 2005.

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***Stroke* is available at http://www.strokeaha.org** **DOI: 10.1161/01.STR.0000181752.16915.5c**

Participants were asked to walk in the corridor at their usual and maximum speed, and while reciting flower names. The time needed to cover 6 m was measured by the photoelectric cells, and walking speed was computed as time divided by 6 m. The 3 measures yielded similar results; we present those for maximum walking speed (MWS). A modified version of the Performance-Oriented Assessment of Mobility Instrument (Tinetti scale) including 13 items (arising from a chair and sitting in a chair, side-by-side, 1 leg and tandem standing balance, standing on toes, pull test, path deviation, turning, step continuity, symmetry, and height) was used to evaluate gait and balance (score 0 to 18).[13]

The following conditions (diabetes mellitus, treated hypercholesterolemia, hip fracture in the previous 2 years, myocardial infarction, angina, bypass cardiac surgery, angioplasty, peripheral vascular disease, Parkinson disease, stroke, and fall in the previous year) were self-reported by the participants during the interview; ischemic heart disease (IHD) was defined as the presence of at least 1 among myocardial infarction, angina, bypass cardiac surgery, and angioplasty. Measures of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were performed in all participants; participants were considered hypertensive in case of antihypertensive drug use or if SBP was ≥160 mm Hg or DBP was ≥95 mm Hg.

Participants underwent cognitive testing and were screened for dementia.[11] A standardized clinical protocol was used to diagnose prevalent cases of dementia in subjects who screened positive. The diagnosis and classification of dementia cases were made by the 3C Study local investigators according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria. Dementia cases were validated by a panel of expert neurologists independently of the 3C Study investigators.[11]

Ultrasound Examination

An ultrasound examination of the carotid arteries was performed in participants ≤85 years of age who visited the study center with a high resolution B-mode system and a 5- to 10-MHz sounding.[14] For financial reasons, it was not proposed to persons included during the last 4 months of the baseline visit. Measurements were performed by nurses or technicians trained at a reference center. The standardized protocol included real-time B-mode scanning of the right and left CCA, carotid bifurcation, and the first 2 cm of internal carotid arteries. The ultrasound system was connected to a computer system that calibrated the ultrasound images and converted them to numerical data. Data were stored on CD-ROMs that were sent to the reference center for centralized measurements of CCA-IMT and diameter of the CCA, carotid plaques, and distensibility of the carotid arteries.

Statistical Analyses

We excluded subjects with conditions that strongly affected motor function (Parkinson disease, dementia, hip fracture in the previous 2 years, stroke, IHD, and peripheral vascular disease). Analysis of covariance and logistic regression were used to study the association between CCA-IMT and walking speed or the modified Tinetti scale. Because of non-normality of CCA-IMT and walking speed distributions, log-transformed variables were used in analysis of covariance; nontransformed means are presented for an easier understanding. In logistic models, MWS and the modified Tinetti scale were the dependent variables and were categorized at the 25th percentile of the distribution, whereas CCA-IMT was the explanatory variable and categorized according to quintiles of the distribution. Because CCA-IMT, MWS, and the modified Tinetti scale were strongly associated with age, sex, and education level, all our analyses were adjusted for these variables. Further adjustment for vascular risk factors was performed (hypertension, history of diabetes mellitus and treated hypercholesterolemia, cigarette smoking, and body mass index [BMI]). Analyses were performed using SAS.[15]

Results

Of 4399 subjects ≤85 years of age who visited the Dijon study center at baseline, an ultrasound examination was performed for 3254; for financial reasons, ultrasound examinations were not performed during the last 4 months of the baseline phase of the study. There were no differences in age, sex, education, or main vascular risk factors between subjects who underwent an ultrasound examination and those who did not. Gait and balance tests were not performed in 98 subjects. After exclusion of 584 subjects who had conditions that impaired motor function, our final sample comprised 2572 subjects, with a measure of CCA-IMT and ≥1 measure available for walking speed (n=2260) or modified Tinetti scale (n=2563).

TABLE 1. General Characteristics of the Participants

Characteristic	n=2572
Mean age (SD)	73.3 (4.7)
Male sex, no. (%)	884 (34)
Education level, no. (%)	
Low	470 (18)
Medium low	1148 (45)
Medium high	490 (19)
High	462 (18)
Mean MMSE score (SD)	27.5 (1.9)
CESD score above threshold, no. (%)	316 (12)
Cigarette smoking, no. (%)	
Never	1638 (64)
Ex-smoker	781 (30)
Current	152 (6)
Diabetes mellitus, no. (%)	165 (6)
Hypertension, no. (%)	1520 (60)
Mean BMI, kg/m^2 (SD)	25.6 (4.0)
Treated hypercholesterolemia, no. (%)	780 (30)
Regular NSAIDS use for joint pain, no. (%)	409 (16)
Fall in the preceding year, no. (%)	
No	2122 (83)
1	288 (11)
>1	143 (6)
Mean modified Tinetti scale (SD)	16.6 (2.2)
Mean usual walking speed, m/s (SD)	1.09 (0.21)
Mean MWS, m/s (SD)	1.54 (0.30)
Mean walking while talking speed, m/s (SD)	0.86 (0.63)
Carotid atherosclerotic plaques, no. (%)	
No	1318 (51)
1	541 (21)
>1	711 (28)
Mean CCA-IMT, mm (SD)	0.692 (0.112)

CESD indicates Center for Epidemiologic Studies Depression scale. Sex-specific thresholds were used (17 in men and 23 in women).

The general characteristics of the participants are shown in Table 1. Table 2 shows the relationship between MWS and selected characteristics. Increasing age and BMI, female gender, decreasing Mini Mental Status Examination (MMSE) score and education level, hypertension, treated hypercholesterolemia, regular nonsteroidal anti-inflammatory drugs (NSAIDs) use for joint pain, depressive symptoms, lower

TABLE 2. Relationship Between Selected Characteristics and MWS

Characteristic	Mean MWS, m/s (SD)	P*
Age, y		$<10^{-4}$
≤73	1.60 (0.29)	
>73	1.46 (0.30)	
Sex		$<10^{-4}$
Female	1.45 (0.27)	
Male	1.70 (0.30)	
Education level		$<10^{-4}$
Low	1.47 (0.29)	
Medium low	1.50 (0.30)	
Medium high	1.57 (0.28)	
High	1.67 (0.31)	
MMSE score		$<10^{-4}$
≥24	1.55 (0.30)	
<24	1.37 (0.29)	
CESD score		$<10^{-4}$
≤threshold	1.56 (0.30)	
>threshold	1.43 (0.30)	
Cigarette smoking		0.59
Never	1.49 (0.29)	
Ex-smoker	1.63 (0.31)	
Current	1.59 (0.32)	
History of diabetes mellitus		0.13
No	1.54 (0.30)	
Yes	1.54 (0.34)	
Hypertension		$<10^{-4}$
No	1.58 (0.30)	
Yes	1.51 (0.30)	
BMI (kg/m^2)		$<10^{-4}$
<30	1.56 (0.30)	
≥30	1.43 (0.30)	
History of treated hypercholesterolemia		0.03
No	1.55 (0.31)	
Yes	1.51 (0.28)	
Regular NSAIDs use for joint pain		$<10^{-4}$
No	1.56 (0.30)	
Yes	1.42 (0.30)	
Fall in the preceding year		0.007
No	1.55 (0.31)	
1	1.48 (0.28)	
>1	1.42 (0.29)	
Modified Tinetti scale†		$<10^{-4}$
≥16	1.59 (0.30)	
<16	1.39 (0.28)	

CESD indicates Center for Epidemiologic Studies Depression.

*Adjusted for age, sex, and education level; †cutoff is the lowest quartile of the distribution.

TABLE 3. The Relationship Between MWS, CCA-IMT, and Carotid Atherosclerotic Plaques

Ultrasound Characteristic	Mean MWS, m/s (SD)	MWS in the Lowest Quartile‡	
		OR (95% CI)*	OR (95% CI)†
CCA-IMT, mm§			
≤0.600	1.61 (0.30)	1.0 (reference)	1.0 (reference)
0.601–0.650	1.54 (0.25)	1.1 (0.8–1.6)	1.0 (0.7–1.5)
0.651–0.710	1.53 (0.30)	1.3 (0.9–1.8)	1.2 (0.9–1.7)
0.711–0.785	1.53 (0.34)	1.7 (1.2–2.4)	1.5 (1.0–2.2)
>0.785	1.47 (0.31)	2.2 (1.6–3.1)	1.9 (1.4–2.8)
Trend *P* value	$<10^{-4}$*/$<10^{-4}$†	$<10^{-4}$	$<10^{-4}$
Carotid atherosclerotic plaques			
No	1.57 (0.30)	1.0 (reference)	1.0 (reference)
1	1.52 (0.30)	1.3 (0.9–1.7)	1.2 (0.9–1.7)
>1	1.50 (0.31)	1.4 (1.1–1.8)	1.3 (1.0–1.7)
Trend *P* value	0.006*/0.03†	0.006	0.01

*Adjusted for age, sex, and education level; †additional adjustment for vascular risk factors (hypertension, history of diabetes and hypercholesterolemia, cigarette smoking, BMI); ‡lowest quartile of the MWS distribution 1.33 m/s; §quintiles.

modified Tinetti score, and falls were associated with lower MWS (Table 2). There was no association between cigarette smoking or diabetes and MWS. Similar relationships were found for the modified Tinetti scale (data not shown), except for diabetes, which was associated with a lower score (odds ratio [OR], 1.8; 95% CI, 1.2 to 2.6; $P=0.003$).

Mean MWS decreased with increasing CCA-IMT; the proportion of subjects with MWS in the lowest quartile increased with CCA-IMT quintiles, as shown by the regular increase in ORs (Table 3); the OR for an increase in 1 SD in CCA-IMT was 1.4 (95% CI, 1.2 to 1.5; $P<10^{-4}$). Adjustment for MMSE score and depressive symptoms had no influence (OR for the last CCA-IMT quintile, 2.2; 95% CI, 1.6 to 3.1; $P<10^{-4}$). Adjustment for vascular risk factors attenuated this relationship moderately (Table 3). The relationship between CCA-IMT and MWS remained after exclusion of diabetic subjects (OR for the last CCA-IMT quintile, 2.1; 95% CI, 1.4 to 3.0; $P<10^{-4}$). In addition, mean MWS decreased with an increasing number of carotid plaques, whereas the proportion of subjects with MWS in the lowest quartile increased (Table 3). Similar findings were observed for usual walking speed and walking while talking speed (data not shown).

A similar association was found between CCA-IMT and the modified Tinetti scale. Mean (SD) CCA-IMT was 0.716 (0.118) mm in subjects with a modified Tinetti score <16 (25th percentile) and 0.685 (0.109) mm in subjects with a score of ≥16 ($P=0.006$). This relationship was no longer significant after adjustment for vascular risk factors ($P=0.16$). In addition, the proportion of subjects with a modified Tinetti score in the first quartile increased with the number of plaques ($P=0.05$); this relationship was no longer significant after adjustment for vascular risk factors ($P=0.18$).

Similar findings were obtained after exclusion of subjects who declared to regularly take NSAIDS for joint pain; mean (SD) MWS was 1.62 (0.30) in the first, 1.56 (0.25) in the second, 1.56 (0.30) in the third, 1.54 (0.34) in the fourth, and 1.49 (0.30) in the last CCA-IMT quintile ($P<10^{-4}$).

Discussion

In this large-scale study of subjects 65 to 85 years of age, we found an association between CCA-IMT or carotid plaques and 2 measures of motor function. The association was attenuated after adjustment for vascular risk factors, thus suggesting that CCA-IMT or carotid plaques are intermediate variables.

The most likely explanation for this association is that individuals with higher CCA-IMT values are at increased risk of cerebral white matter hyperintensities (WMHs) and silent infarcts.[16–18] Previous studies have shown that WMHs are more common in subjects performing worse on several measures of gait and balance; for instance, in the Cardiovascular Health Study, several measures of motor function were associated with WMHs in subjects ≥65 years of age.[17] This finding was confirmed in smaller cross-sectional[19] and longitudinal studies.[20,21] Alternatives mechanisms (eg, peripheral diabetic neuropathy) are less likely because adjustment for diabetes or exclusion of diabetic subjects did not modify our findings. Finally, the associations that we observed remained unchanged after adjustment for MMSE level, thus suggesting that they were independent of cognitive function.

We used CCA-IMT as a vascular marker because it is considered to be a cumulative measure of long-term exposure to vascular risk factors, in particular hypertension.[5] CCA-IMT can be measured noninvasively and with good reproducibility using ultrasonography, is less expensive to perform in large-scale studies than MRI, and can be repeated more easily. Measures of motor function were associated with CCA-IMT and carotid plaques, but the association was more pronounced for CCA-IMT than for carotid plaques. If the hypothesis that this association is mediated by WMHs is correct, a possible explanation for this stronger association with CCA-IMT is that hypertension, in addition to age, is the main risk factor for WMHs and increased CCA-IMT, whereas plaques probably reflect the influence of several other risk factors.[22]

Walking speed is a reproducible measure[23] and a good predictor of functional dependence onset of in the elderly.[2,12] To increase reproducibility, we measured walking speed using an automatic device. The Tinetti scale describes characteristics of gait and balance and has been shown to predict falls and functional dependence.[24–26] To shorten the duration of the test, we used a modified version including fewer items. Because the scale distribution was highly skewed, we analyzed the data after categorization of this variable, whereas walking speed could be analyzed as a continuous variable.

Subjects excluded from the analyses experienced conditions that impaired motor function; mean (SD) MWS was 1.47 (0.32) in subjects excluded versus 1.54 (0.30) in subjects included in the analyses ($P<10^{-4}$). In addition, diseases associated with increased CCA-IMT and slower walking speed (eg, IHD and stroke) may be a source of confounding. The diagnoses that led to exclusion from the study were self-reported, and self-report may be more accurate for some conditions (eg, myocardial infarction and coronary revascularization) than others (eg, angina and peripheral vascular disease).[27] However, we believe that our findings are robust because the number of subjects with angina or peripheral vascular disease (who did not report another cardiovascular disease) was small. In addition, excluding subjects or not from the analyses did not affect our findings because the association between motor tests and CCA-IMT was also present in subjects excluded (data not shown). Finally, excluding subjects who reported regular NSAIDs use for joint pain, and therefore likely to experience a form of arthritis, did not affect our findings either.

A limitation of the study is its cross-sectional nature. The cohort is currently being followed, and longitudinal analyses will be performed in the future. In addition, participants were subjects 65 to 85 years of age who accepted to participate to the study and were able to come to the study center; they differed from the French general population in terms of age, sex, and socioeconomic level.[11] However, the associations observed in our study between CCA-IMT and vascular risk factors (data not shown) or between gait and balance measures and other clinical characteristics are very similar to those reported in the literature. In addition, the relationships that we observed were all characterized by dose–effect relations, which is reassuring with respect to potential selection biases. Finally, all the participants did not undergo B-mode ultrasound examination. However, the number of examinations was preplanned based on financial considerations. It is unlikely that it may have been a source of bias because the order of inclusion of the participants was random; therefore, we did not find differences between subjects who underwent B-mode ultrasound examination and those who did not.

Our findings are in line with the involvement of vascular risk factors in cognitive decline and dementia.[28] They are based on a large sample of community-dwelling subjects 65 to 85 years of age and suggest that vascular risk factors play an important and under-recognized role in motor function in the elderly. If confirmed, they also suggest that the control of vascular risk factors may be an opportunity to prevent gait disorders in the elderly.[29]

Acknowledgments

The 3C Study is mainly supported by the Fondation pour la Recherche Médicale and the Sanofi-Synthélabo Company.

References

1. Bennett DA, Beckett LA, Murray AM, Shannon KM, Goetz CG, Pilgrim DM, Evans DA. Prevalence of parkinsonian signs and associated mortality in a community population of older people. *N Engl J Med*. 1996;334:71–76.
2. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med*. 1995;332:556–561.
3. Wilson RS, Schneider JA, Beckett LA, Evans DA, Bennett DA. Progression of gait disorder and rigidity and risk of death in older persons. *Neurology*. 2002;58:1815–1819.
4. Liston R, Mickelborough J, Bene J, Tallis R. A new classification of higher level gait disorders in patients with cerebral multi-infarct states. *Age Ageing*. 2003;32:252–258.
5. Simon A, Gariepy J, Chironi G, Megnien JL, Levenson J. Intima-media thickness: a new tool for diagnosis and treatment of cardiovascular risk. *J Hypertens*. 2002;20:159–169.

6. Persson J, Formgren J, Israelsson B, Berglund G. Ultrasound-determined intima-media thickness and atherosclerosis. Direct and indirect validation. *Arterioscler Thromb*. 1994;14:261–264.
7. Zureik M, Ducimetiere P, Touboul PJ, Courbon D, Bonithon-Kopp C, Berr C, Magne C. Common carotid intima-media thickness predicts occurrence of carotid atherosclerotic plaques: longitudinal results from the Aging Vascular Study (EVA) study. *Arterioscler Thromb Vasc Biol*. 2000;20:1622–1629.
8. van der Meer IM, Bots ML, Hofman A, del Sol AI, van der Kuip DA, Witteman JC. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. *Circulation*. 2004;109:1089–1094.
9. Hollander M, Hak AE, Koudstaal PJ, Bots ML, Grobbee DE, Hofman A, Witteman JC, Breteler MM. Comparison between measures of atherosclerosis and risk of stroke: the Rotterdam Study. *Stroke*. 2003;34: 2367–2372.
10. Nathan DM, Lachin J, Cleary P, Orchard T, Brillon DJ, Backlund JY, O'Leary DH, Genuth S. Intensive diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. *N Engl J Med*. 2003; 348:2294–2303.
11. 3C Study Group. Vascular factors and risk of dementia: design of the Three-City Study and baseline characteristics of the study population. *Neuroepidemiology*. 2003;22:316–325.
12. Shinkai S, Watanabe S, Kumagai S, Fujiwara Y, Amano H, Yoshida H, Ishizaki T, Yukawa H, Suzuki T, Shibata H. Walking speed as a good predictor for the onset of functional dependence in a Japanese rural community population. *Age Ageing*. 2000;29:441–446.
13. Tinetti ME, Liu WL, Claus EB. Predictors and prognosis of inability to get up after falls among elderly persons. *J Am Med Assoc*. 1993;269: 65–70.
14. Zureik M, Gariepy J, Courbon D, Dartigues JF, Ritchie K, Tzourio C, Alperovitch A, Simon A, Ducimetiere P. Alcohol consumption and carotid artery structure in older French adults: the Three-City Study. *Stroke*. 2004;35:2770–2775.
15. SAS. Cary, NC, USA: 1999.
16. Bots ML, van Swieten JC, Breteler MM, de Jong PT, van Gijn J, Hofman A, Grobbee DE. Cerebral white matter lesions and atherosclerosis in the Rotterdam Study. *Lancet*. 1993;341:1232–1237.
17. Longstreth WT Jr, Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA, Enright PL, O'Leary D, Fried L. Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study. *Stroke*. 1996;27:1274–1282.
18. Vermeer SE, Den Heijer T, Koudstaal PJ, Oudkerk M, Hofman A, Breteler MM. Incidence and risk factors of silent brain infarcts in the population-based Rotterdam Scan Study. *Stroke*. 2003;34:392–396.
19. Guttmann CR, Benson R, Warfield SK, Wei X, Anderson MC, Hall CB, Abu-Hasaballah K, Mugler JP III, Wolfson L. White matter abnormalities in mobility-impaired older persons. *Neurology*. 2000;54:1277–1283.
20. Baloh RW, Ying SH, Jacobson KM. A longitudinal study of gait and balance dysfunction in normal older people. *Arch Neurol*. 2003;60: 835–839.
21. Whitman GT, Tang Y, Lin A, Baloh RW, Tang T. A prospective study of cerebral white matter abnormalities in older people with gait dysfunction. *Neurology*. 2001;57:990–994.
22. Spence JD. Carotid intima-media thickness and cognitive decline: what does it mean for prevention of dementia? *J Neurol Sci*. 2004;223: 103–105.
23. Nagasaki H, Itoh H, Hashizume K, Furuna T, Maruyama H, Kinugasa T. Walking patterns and finger rhythm of older adults. *Percept Mot Skills*. 1996;82:435–447.
24. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. *J Am Geriatr Soc*. 1986;34:119–126.
25. Raiche M, Hebert R, Prince F, Corriveau H. Screening older adults at risk of falling with the Tinetti balance scale. *Lancet*. 2000;356:1001–1002.
26. Gill TM, Williams CS, Tinetti ME. Assessing risk for the onset of functional dependence among older adults: the role of physical performance. *J Am Geriatr Soc*. 1995;43:603–609.
27. Heckbert SR, Kooperberg C, Safford MM, Psaty BM, Hsia J, McTiernan A, Gaziano JM, Frishman WH, Curb JD. Comparison of self-report, hospital discharge codes, and adjudication of cardiovascular events in the Women's Health Initiative. *Am J Epidemiol*. 2004;160:1152–1158.
28. Gorelick PB. Risk factors for vascular dementia and Alzheimer disease. *Stroke*. 2004;35:2620–2622.
29. Martin MP, O'Neill D. Vascular higher-level gait disorders—a step in the right direction? *Lancet*. 2004;363:8.