Impact of Nocturia on Bone Fracture and Mortality in Older Individuals: A Japanese Longitudinal Cohort Study

Haruo Nakagawa,* Kaijun Niu, Atsushi Hozawa, Yoshihiro Ikeda, Yasuhiro Kaiho, Kaori Ohmori-Matsuda, Naoki Nakaya, Shinichi Kuriyama, Satoru Ebihara, Ryoichi Nagatomi, Ichiro Tsuji and Yoichi Arai

From the Departments of Urology (HN, YI, YK, YA), Medicine and Science in Sports and Exercise (KN, RN) and Public Health and Forensic Medicine (AH, KOM, NN, SK, IT), Tohoku University Graduate School of Medicine and Department of Geriatrics and Gerontology, Institute of Development, Aging and Cancer, Tohoku University (SE), Sendai, Japan

Purpose: We evaluated the association of nocturia with fracture and death in a large, community based sample of Japanese individuals 70 years old or older.

Materials and Methods: The baseline in this population based study was determined in 2003 by an extensive health interview with each participant. In this study we followed 784 individuals with a mean ± SD age of 76.0 ± 4.6 years (range 70 to 97). Information on mortality and fracture during the study period was provided by the National Health Insurance system and details on fractures were collected from medical records. We compared the risk of bone fracture and death with or without nocturia in a multivariate Cox proportional hazard model.

Results: Nocturia (2 or greater voids per night) was present in 359 of the 784 participants (45.7%). Fracture was observed in 41 cases, including 32 fall related cases. For all fractures and fall related fractures with nocturia the HR was 2.01 (95% CI 1.04–3.87) and 2.20 (95% CI 1.04–4.68, each $p = 0.04$). Death occurred in 53 cases. The mortality rate in individuals with nocturia was significantly higher than in those without nocturia. For mortality in patients with nocturia the age-gender adjusted HR was 1.91 (95% CI 1.07–3.43, $p = 0.03$). Even when further adjusted for diabetes, smoking status, history of coronary disease, renal disease and stroke, tranquilizers, hypnotics and diuretics, the positive relationship was unchanged (HR 1.98, 95% CI 1.09–3.59, $p = 0.03$).

Conclusions: During a 5-year observation period elderly individuals with nocturia were at greater risk for fracture and death than those without nocturia.

Key Words: urinary bladder; nocturia; fractures, bone; mortality; aged

Abbreviations and Acronyms

BMI = body mass index

NHI = National Health Insurance

QOL = quality of life

SWS = slow wave sleep

Submitted for publication November 27, 2009.

Study received Tohoku University Graduate School of Medicine ethics committee approval.

Supported by Grant 21592064 for Research Conducted by the Japanese Society for Promotion of Science from the Ministry of Education, Culture, Sports, Science and Technology, Japan, research grants from Chiyoda Mutual Life Foundation and Universe Foundation, and Ferring Pharmaceuticals.

* Correspondence: 1-1 Seiryo Aoba-ku, Sendai, Miyagi 980-8574, Japan (telephone: +81-22-717-7278; FAX: +81-22-717-7283; e-mail: bob@uro.med.tohoku.ac.jp).

NOCTURIA is defined by the International Continence Society as the complaint that the individual awakens at night 1 or more times to void.[1] The prevalence of nocturia increases with age, such that around 70% of individuals 55 years old or older void at least once per night.[2] Despite or perhaps due to this high prevalence in society nocturia is frequently dismissed as an inevitable consequence of aging and, thus, it remains untreated in many individuals.[3]

Nocturia is the leading cause of sleep fragmentation in older adults.[3] Due to its chronic impact on the sleep cycle it can have serious consequences for daytime function, mood, QOL and health.[4–7] The average first nocturia episode occurs within 2 to 3 hours of going to bed. Awakening at this time is likely to interrupt SWS, which is the deep sleep phase believed to be most restorative.[8] Interrupting SWS is associated with a number of nega-

0022-5347/10/1844-1413/0
THE JOURNAL OF UROLOGY®

Vol. 184, 1413-1418, October 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.05.093

tive sequelae, including impaired normal glucose homeostasis.[9] Those with nocturia report significantly worse QOL and health than those without nocturia.[2,7,10,11]

Particularly in older individuals falls are a major health problem and the principal cause of death from injury in this group.[12] Previous studies suggest that nocturia may be an important risk factor for falls in men older than 65 years.[13] In a community based study the risk of falling was more than doubled in participants with at least 3 episodes of nocturia per night.[12] Others determined that the risk of hip fracture is independently increased by increased nocturnal micturition and nocturnal urine output.[14] Hip fracture in the elderly population and bone fracture in general may lead to severe complications and in some cases death. For example, there is an overall 5.3% in-hospital mortality rate after hip fracture.[14]

Nocturia is associated with a greater risk of mortality.[15] The increased risk of fracture with nocturia may be a mechanism by which the mortality risk increases. Also, nocturia is associated with several comorbidities, such as diabetes and coronary disease. Thus, the increased mortality rate in individuals with nocturia may be at least partially attributable to the increased incidence of those health issues. However, in a study of patients with coronary disease nocturia was a significant independent predictor of mortality.[16] We evaluated the association of nocturia with fracture and death in a large Japanese, community based sample of individuals 70 years old or older.[17–20]

MATERIALS AND METHODS

Study Participants

The Tsurugaya Project was a community based, comprehensive geriatric assessment that recruited individuals ages 70 years old or older who lived in the Tsurugaya area of Sendai, a major city in the Tohoku area of Japan. At the time of the study (July to August 2003) 2,925 individuals 70 years old or older lived in Tsurugaya. All were invited to participate in the assessment, which included medical status, physical function, cognitive function and dental status. Of those invited 948 individuals attended the assessment and provided informed consent for data analysis, of whom 784 who had joined the NHI system and agreed to a medical record review were included in this study. The study protocol was approved by the Tohoku University Graduate School of Medicine ethics committee.

Data

Collection. Information on nocturia was collected by trained interviewers. They asked participants, "During the last month how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?" Those who reported voiding 2 or greater times per night were defined as having nocturia since previous studies showed that individuals with 2 or more voids per night have significantly worse QOL and health than those without nocturia.[2,7,10,11]

Information on smoking status, drinking status, medication and disease history was obtained via questionnaire. The drug information was confirmed by a qualified pharmacist.[20] To evaluate the ability of participants to maintain balance we measured functional reach.[21,22] This test measures how far a participant can reach forward beyond arm length and maintain a fixed base of support while standing without losing balance. We attempted the test twice. The longer reach result was used in analysis.

Followup. We prospectively collected data on medical care, expenditures and mortality in all individuals in the cohort study from August 2003 to March 2008. We obtained NHI claims history files from the Miyagi NHI Association. The files included the number of outpatient visits and days of inpatient care, charges for outpatient and inpatient care, and mortality data. When a beneficiary was withdrawn from the NHI, the date and reason were coded on a NHI withdrawal history file. This file identified survival and emigration status in each participant. NHI claims and withdrawal history files were linked with our baseline survey data file based on the beneficiary identification number. The incidence and causes of fracture were investigated using the NHI claim record and patient hospital records. NHI records were used to identify the hospital where patients were admitted. We then visited the hospital and reviewed hospital records to confirm the diagnosis, incident day and reason for fracture.

Statistical Analysis

We assessed the relationship of baseline characteristics with demographic variables and the nocturia risk using the t and chi-square tests, and multivariate logistic regression analysis. Variables under consideration were gender, age, high blood glucose, history of coronary disease, nephropathy, diabetes, malignant disease and smoking status. We compared the fracture risk with or without nocturia using the multivariate Cox proportional hazard model adjusted for age, gender, BMI, tranquilizers, hypnotics, diuretics and functional reach. Differences in mortality with time according to the presence or absence of nocturia were assessed by Kaplan-Meier curves and statistical significance was calculated with the log rank test. We compared the risk of mortality with or without nocturia using an age-gender adjusted Cox proportional hazard model. We also used a model adjusting for age, gender, BMI, diabetes, smoking status, history of coronary disease, renal disease and malignant disease, tranquilizers, hypnotics and diuretics. Statistically significant differences were considered at $p < 0.05$. SAS®, version 9.1 was used for analyses.

RESULTS

Of the 784 participants 427 (54.5%) were female. Overall mean ± SD age was 76.0 ± 4.6 years (range 70 to 97). In those without and with nocturia mean age was 75.2 ± 4.2 and 77.0 ± 4.8 years (OR 1.9, 95% CI 1.05–1.13, $p < 0.01$), and mean BMI was

24.1 ± 3.2 and 24.1 ± 3.5 kg/m^2 (HR 1.02, 95% CI 0.97–1.06, p = 0.82), respectively.

Nocturia

Nocturia (2 or greater voids per night) was present in 359 of 784 cases (45.8%). **Table 1** shows the results of multivariate analysis of the effect of demographic and baseline variables on nocturia prevalence. Male gender, older age, coronary disease history and malignant disease were associated with a significantly increased risk of nocturia. Current smoking was associated with a significantly decreased risk of nocturia.

Fracture

We noted fracture in 41 cases, of which 32 were fall related. Eight, 6 and 21 patients had fracture of the arm, lower limb and hip, respectively. Six fractures were classified as other.

The cumulative incidence rate of fracture was significantly higher in individuals with vs without nocturia (26 of 359 or 7.2% vs 15 of 425 or 3.5%, **fig. 1**). Similarly the cumulative incidence rate of fall related fracture was significantly higher in those with vs without nocturia (21 of 359 or 5.8% vs 11 of 425 or 2.6%). Multivariate HR adjusted for age, BMI, tranquilizers, hypnotics, diuretics and functional reach in all fractures in men, women and all participants with nocturia was 2.61 (95% CI 0.76–8.95, p = 0.13), 2.07 (95% CI 0.95–4.51, p = 0.07) and 2.01 (95% CI 1.04–3.87, p = 0.04), respectively (**table 2**). The HR for fall related fracture in all participants was 2.20 (95% CI 1.04–4.68, p = 0.04).

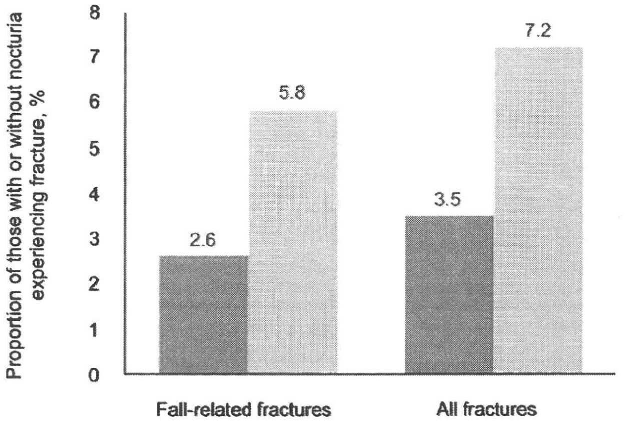

Figure 1. Incidence of all and fall related fractures in 359 patients with (light blue bars) and in 425 without (dark blue bars) nocturia was significantly higher in former (each p = 0.03).

Mortality

The cumulative mortality rate was higher in individuals with than without nocturia (35 of 359 or 9.7% vs 18 of 425 or 4.2%). **Figure 2** shows Kaplan-

Table 1. *Baseline characteristics by nocturia status*

	No. No Nocturia (%)	No. Nocturia (%)	p Value (t or chi-square test)	OR (95% CI)
Gender:			0.02	
M	177 (41.7)	180 (50.1)		Referent
F	248 (58.4)	179 (49.9)		0.64 (0.42–0.99)
High blood glucose:			0.2	
No	337 (79.3)	271 (75.5)		Referent
Yes	88 (20.7)	88 (24.5)		1.14 (0.80–1.63)
Tranquilizers:			0.32	
No	378 (88.9)	311 (86.6)		Referent
Yes	47 (11.1)	48 (13.4)		1.14 (0.80–1.63)
Hypnotics:			0.45	
No	389 (91.5)	323 (90.0)		Referent
Yes	36 (8.5)	36 (10.0)		1.37 (0.87–2.15)
Diuretics:			0.18	
No	405 (95.3)	334 (93.0)		Referent
Yes	20 (4.7)	25 (7.0)		1.19 (0.63–2.27)
Renal disease history:			0.47	
No	396 (93.2)	339 (94.4)		Referent
Yes	29 (6.8)	20 (5.6)		0.71 (0.38–1.32)
Myocardial infarction history:			<0.01	
No	394 (92.7)	308 (85.8)		Referent
Yes	31 (7.3)	51 (14.2)		1.87 (1.14–3.08)
Malignant disease history:			<0.01	
No	396 (93.2)	311 (86.6)		Referent
Yes	29 (6.8)	48 (13.4)		2.15 (1.30–3.57)
Smoking status:				
Never	258 (60.7)	196 (54.6)	0.02	Referent
Past	112 (26.4)	129 (35.9)		1.08 (0.69–1.69)
Current	48 (11.3)	27 (7.5)		0.59 (0.32–1.08)

Table 2. *All fracture and all cause mortality by nocturia status*

	No. Nighttime Voids		
	1 or Less	2 or Greater	p Value
	*All fracture**		
Men:	174	178	
No. fracture	4	9	
HR (95% CI)	1.00	2.61 (0.76–8.95)	0.13
Women:	237	162	
No. fracture	11	17	
HR (95% CI)	1.00	2.07 (0.95–4.51)	0.07
Overall:	425	359	
No. fracture	15	26	
HR (95% CI)	1.00	2.01 (1.04–3.87)	0.04
	All cause mortality†		
No. deaths	18	35	
HR (95% CI):			
Crude model	1.00	2.43 (1.38–4.30)	<0.01
Model 2†	1.00	1.91 (1.07–3.43)	0.03
Model 3‡	1.00	1.98 (1.09–3.59)	0.02

* Adjusted for age, gender, BMI, tranquilizers, hypnotics, diuretics and functional reach.

† Adjusted for age, gender and BMI.

‡ Adjusted for model 2 plus diabetes, smoking status, coronary disease, renal disease, stroke, tranquilizers, hypnotics and diuretics.

Meier mortality curves. There was a significant difference between individuals with and without nocturia (p = 0.0015).

The age-gender adjusted HR for death in patients with 2 or greater episodes of nocturia per night was 1.91 (95% CI 1.07–3.43, p = 0.03). In the additional, more comprehensive model adjusting for age, gender, BMI, diabetes, smoking status, history of coronary disease, renal disease and stroke, tranquilizers, hypnotics and diuretics nocturia still independently predicted increased mortality risk (HR 1.98, 95% CI 1.09–3.59; p = 0.03, **table 2**).

DISCUSSION

In this 5-year study we considered potential risk factors for nocturia and the subsequent effect of nocturia on the incidence of fracture and death in individuals 70 years old or older. Key findings were that nocturia (2 or greater voids per night) was present in almost half of the population and it was an independent risk factor for fracture and for increased mortality.

In a previous 5-year study nocturia was identified as an independent risk factor for hip fracture.[23] Consistent with this finding we found that the fracture prevalence more than doubled in patients with nocturia. Generally women are much more likely to have osteoporosis than men, which significantly increases the risk of fracture.[24] Also, the physiology of nocturia differs between men and women because of the prostate. However, there is same tendency that nocturia correlates with fracture in men only (p = 0.13) and in women only (p = 0.07). When considering fracture of any cause, all participants (men and women) with nocturia were at increased risk on multivariate adjusted analysis.

The correlation between the number of nighttime voids and the fracture prevalence was not a linear proportional correlation (data not shown). This may have been due to the multifactorial etiology of fracture and the relatively small number of events. On the other hand, falls are a major health problem in older people in general[25] and nocturia seems to be an important additional contributor to the fracture risk in this age group. Since details on time of day were not available, it was not possible to ascertain whether injuries were sustained during the night and as a direct result of nighttime visits to the toilet. Patients with nocturia may be more at risk for daytime injury due to the fragmented sleep and fatigue caused by nocturnal voiding. Fractures of any cause have a major impact on QOL. Thus, any lifestyle modifications or treatments that decrease nocturia episodes and so decrease the incidence of falls and subsequent fracture would be beneficial in terms of decreasing the economic and personal burdens involved.

We also found an increased risk of death in elderly patients with nocturia. Nocturia can arise from many physiological conditions. Thus, the possibility exists that the causes of the increased nocturia rate also caused the increased mortality rate. However, on analysis adjusted for a wide range of medical conditions and demographic variables nocturia was an independent predictor of death. This suggests an alternative underlying mechanism that

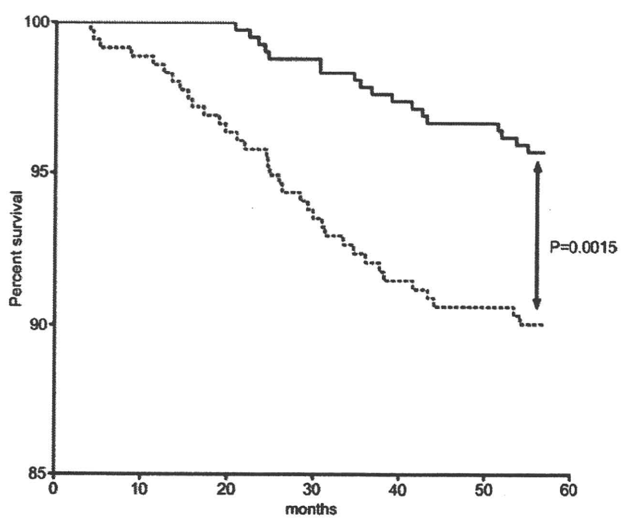

Figure 2. Kaplan-Meier estimates show significantly lower mortality in patients without (solid curve) than with (dotted curve) nocturia (log rank test p = 0.0015), defined as 1 or fewer vs 2 or greater voids per night, respectively.

may be directly related to nocturia, and increased fracture and/or the fragmented sleep caused by the need to wake to void repeatedly at night. Poor sleep is associated with poor health and SWS interruption has an effect on the regulation of physiological processes, such as glucose metabolism[9] and immunity.[26] Thus, nocturia may increase the risk of death by its impact on sleep and subsequent health implications.

In the elderly population those with nocturia appear to be at increased risk for fracture and death regardless of a range of possible comorbid conditions. Thus, nocturia may be a marker of more serious underlying conditions in some patients as well as a carrier of additional risk in terms of 1) injury possibly directly related to nighttime visits to the toilet and 2) an independent relationship with increased mortality possibly mediated by the increase in injuries and/or the effects of poor sleep on health.

Regardless of the true mechanisms of the relationship of nocturia with fracture and death the existence of an association between the condition and serious consequences in the patient is clear. Thus, this should not be considered a trivial and/or inevitable consequence of aging. Rather, nocturia deserves thorough evaluation of the underlying causes in each patient. Clinicians should actively monitor nocturia in older patients and consider whether those complaining of insomnia may in fact experience sleep disturbance due to nighttime voiding. After the specific etiology of nocturia is established in each individual appropriate treatment targeting the relevant contributing factors should be offered to minimize the repercussions of the condition and any possible underlying factors for patient health and overall QOL.[11]

Treatment for nocturia is available.[27] It has the potential to decrease these risks in patients with nocturia by decreasing the number of voids per night, decreasing fragmentation of the sleep cycle and increasing the potential for uninterrupted SWS. Treatment selection should be based on the etiology of the condition in each patient. As discussed, there are many possible contributors to nocturia but nocturnal polyuria is present in up to about 83% of patients[28,29] and is especially common in the elderly population. This is believed to be related to decreased secretion of antidiuretic hormone with age.[30] Further studies of the impact of treatment to effectively decrease the frequency of nocturia on the fracture and mortality rates would be of interest and extend the current evidence base supporting the benefits of treatment for this condition. In conclusion, in this 5-year cohort study in an elderly, community dwelling population in Japan those with nocturia (2 or greater voids per night) were at increased risk for fracture and increased risk for death even when multivariate analysis was adjusted for several possible contributing comorbidities and lifestyle factors.

ACKNOWLEDGMENTS

Dr. Caroline Loat provided comments.

REFERENCES

1. van Kerrebroeck P, Abrams P, Chaikin D et al: The standardisation of terminology in nocturia: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002; **21:** 179.
2. van Dijk L, Kooij DG and Schellevis FG: Nocturia in the Dutch adult population. BJU Int 2002; **90:** 644.
3. Bliwise DL, Foley DJ, Vitiello MV et al: Nocturia and disturbed sleep in the elderly. Sleep Med 2009; **10:** 540.
4. Cote KA, Milner CE, Osip SL et al: Waking quantitative electroencephalogram and auditory event-related potentials following experimentally induced sleep fragmentation. Sleep 2003; **26:** 687.
5. Ohayon MM: Nocturnal awakenings and comorbid disorders in the American general population. J Psychiatr Res 2008; **43:** 48.
6. Asplund R, Marnetoft SU, Selander J et al: Nocturia in relation to somatic health, mental health and pain in adult men and women. BJU Int 2005; **95:** 816.
7. Yu HJ, Chen FY, Huang PC et al: Impact of nocturia on symptom-specific quality of life among community-dwelling adults aged 40 years and older. Urology 2006; **67:** 713.
8. Stanley N: The underestimated impact of nocturia on quality of life. Eur Urol, suppl., 2005; **4:** 17.
9. Tasali E, Leproult R, Ehrmann DA et al: Slow-wave sleep and the risk of type 2 diabetes in humans. Proc Natl Acad Sci U S A 2008; **105:** 1044.
10. Hernandez C, Estivill E, Prieto M et al: Nocturia in Spanish patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH). Curr Med Res Opin 2008; **24:** 1033.
11. Tikkinen KA, Johnson TM 2nd, Tammela TL et al: Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol 2009; **57:** 363.
12. Stewart RB, Moore MT, May FE et al: Nocturia: a risk factor for falls in the elderly. J Am Geriatr Soc 1992; **40:** 1217.
13. Parsons JK, Mougey J, Lambert L et al: Lower urinary tract symptoms increase the risk of falls in older men. BJU Int 2009; **104:** 63.
14. Alvarez-Nebreda ML, Jimenez AB, Rodriguez P et al: Epidemiology of hip fracture in the elderly in Spain. Bone 2008; **42:** 278.
15. Asplund R: Mortality in the elderly in relation to nocturnal micturition. BJU Int 1999; **84:** 297.
16. Bursztyn M, Jacob J and Stessman J: Usefulness of nocturia as a mortality risk factor for coronary heart disease among persons born in 1920 or 1921. Am J Cardiol 2006; **98:** 1311.
17. Kuriyama S, Hozawa A, Ohmori K et al: Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project 1. Am J Clin Nutr 2006; **83:** 355.
18. Kuriyama S, Koizumi Y, Matsuda-Ohmori K et al: Obesity and depressive symptoms in elderly Japanese: the Tsurugaya Project. J Psychosom Res 2006; **60:** 229.
19. Hozawa A, Ohmori K, Kuriyama S et al: C-reactive protein and peripheral artery disease among Jap-

anese elderly: the Tsurugaya Project. Hypertens Res 2004; **27:** 955.

20. Kikuchi A, Niu K, Ikeda Y et al: Association between physical activity and urinary incontinence in a community-based elderly population aged 70 years and over. Eur Urol 2007; **52:** 868.

21. Suzuki T, Kim H, Yoshida H et al: Randomized controlled trial of exercise intervention for the prevention of falls in community-dwelling elderly Japanese women. J Bone Miner Metab 2004; **22:** 602.

22. Ingemarsson AH, Frandin K, Hellstrom K et al: Balance function and fall-related efficacy in patients with newly operated hip fracture. Clin Rehabil 2000; **14:** 497.

23. Asplund R: Hip fractures, nocturia, and nocturnal polyuria in the elderly. Arch Gerontol Geriatr 2006; **43:** 319.

24. Schuit SC, van der Klift M, Weel AE et al: Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. Bone 2004; **34:** 195.

25. Baker SP and Harvey AH: Fall injuries in the elderly. Clin Geriatr Med 1985; **1:** 501.

26. Opp MR: Sleeping to fuel the immune system: mammalian sleep and resistance to parasites. BMC Evol Biol 2009; **9:** 8.

27. van Kerrebroeck P, Rezapour M, Cortesse A et al: Desmopressin in the treatment of nocturia: a double-blind, placebo-controlled study. Eur Urol 2007; **52:** 221.

28. Chang SC, Lin AT, Chen KK et al: Multifactorial nature of male nocturia. Urology 2006; **67:** 541.

29. Abrams PA, Mattiasson A, Van Kerrebroeck P et al: Is nocturnal polyuria a key factor in nocturia? Neurourol Urodyn 2004; **23:** 466.

30. Akiyama T, Hirayama A, Fujimoto K et al: Cutoff value of urinary arginine vasopressin for nocturnal polyuria in elderly men. Urology 2007; **69:** 98.

Geriatrics Gerontology International 1st Impact Factor in June 2010 Medline Indexed

Geriatr Gerontol Int 2010

ORIGINAL ARTICLE

Impact of physical activity and performance on medical care costs among the Japanese elderly

Guang Yang,[1,2] Kaijun Niu,[1] Kazuki Fujita,[3] Atsushi Hozawa,[4] Kaori Ohmori-Matsuda,[4] Shinichi Kuriyama,[4] Naoki Nakaya,[4] Satoru Ebihara,[5] Tatsuma Okazaki,[5] Hiu Guo,[1] Chihaya Miura,[1] Hideko Takahashi,[4] Hiroyuki Arai,[5] Ichiro Tsuji[4] and Ryoichi Nagatomi[1]

[1]Division of Biomedical Engineering for Health and Welfare, Tohoku University Graduate School of Biomedical Engineering, [4]Division of Epidemiology, Departments of Public Health and Forensic Medicine and [5]Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, [3]Institute for Higher Education Research Practice, Osaka University, Suita, Osaka, Japan; and [2]Department of Sports Sciences, Shen Yang Normal University, Shen Yang, China

Aim: Physical activity (PA) is known to be inversely associated with medical care costs. The amount of PA is strongly associated with the level of physical performance among the elderly population. Therefore, it is possible that known relation between PA and medical care merely shows the relation between physical performance and medical care. To know whether PA itself relates to medical care, considering physical performance is necessary. The aim of this study was to ascertain the impact of PA on medical care expenditure by considering the physical performance in an elderly community-dwelling population.

Methods: We investigated 483 subjects who did not have any history of diseases relating to limited PA and who completed both a self-administered questionnaire including questions on PA and underwent a physical performance measurement. We ascertained the total medical care costs through a computerized linkage with claims lodged between August 2002 and March 2008 with the Miyagi National Health Insurance Association.

Results: The physical performance was positively associated with their level of PA. After multivariate adjustment for covariables including the levels of physical performance, the per capita medical care costs were found to be $US 827.3 (598.0–1056.7) (mean, 95% confidence interval), $US 711.1 (476.4–945.8) and $US 702.0 (461.6–942.4) (*P* for linear trend = 0.02) per month for those who had the lowest, average and the highest level of PA, respectively.

Conclusion: This prospective study indicates that a higher level of PA is associated with lower medical care costs among the Japanese elderly irrespective of physical performance. **Geriatr Gerontol Int 2010; 10: ••–••.**

Keywords: community-dwelling elderly population, medical care costs, physical activity, physical performance.

Introduction

The rising medical care costs associated with the growth of the elderly population is an ongoing problem worldwide.[1,2] In the 2005 Japanese census report, the proportion of the elderly population in the total population of the country was 20.1%. This proportion is expected to

Accepted for publication 3 August 2010.

Correspondence: Dr Ryoichi Nagatomi MD PhD, Division of Biomedical Engineering for Health and Welfare, Tohoku University Graduate School of Biomedical Engineering, 2-1 Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan. Email: nagatomi@med.tohoku.ac.jp

doi: 10.1111/j.1447-0594.2010.00651.x

reach 35.7% by 2050.[3] In the 2002 Health and Welfare Statistics Association survey, 50.4% of the total national medical care costs were incurred by elderly individuals over 65 years of age.[4] According to the survey, the average per capita monthly medical care costs were $US 1284 for the under-65 age group and $US 5536 for the over-65 age group; that is, the costs for the latter group were five times higher than those for the former.

A sedentary lifestyle has been found to be associated with an increased risk of developing various chronic diseases and mortality.[5–8] Actually, several studies have reported that physical activity (PA) is inversely associated with medical care costs.[9–11] The promotion of regular PA may lead to a reduction in medical care costs. The amount of PA, however, is strongly associated with the level of physical performance, especially in the elderly population.[12–17] Therefore, it is natural to assume that physical performance would be an important mediator in the relationship between PA and medical care costs. Thus, careful consideration of this potentially important confounding or effect-modifying factor is needed when analyzing the data. However, to our knowledge, no previous studies have investigated the impact of physical activity on medical care expenditure using stratified analyses of physical performance levels.

We thus designed a cohort study of National Health Insurance (NHI) beneficiaries to investigate the link between PA levels and medical care costs in association with physical performance in an elderly Japanese community-dwelling population.

Methods

Study participants

Our data were derived from a prospective observation of NHI beneficiaries in suburban Japan through August 2002 to March 2008. In 2002, there were 2730 individuals aged 70 years and older living in Tsurugaya, a residential area in one of the major cities in northern Japan, Sendai City. We invited all of these individuals to participate in a comprehensive geriatric assessment[18] in which the physical, mental and social functioning of elderly people was examined to assess the early deterioration that could result in the need for long-term care and thus to promote healthy aging. Of those invited, 1178 gave written informed consent to being included in the structured survey. Of these 1178, we investigated 969 persons who agreed to respond to a questionnaire on medical care costs, the coverage of these costs under the NHI system, and medical care utilization derived from claim history files. The comprehensive health and lifestyle information for each subject at baseline allowed us to adjust for a variety of potential confounders. The protocol of this study was approved by the Institutional Review Board of the Tohoku University Graduate School of Medicine.

We excluded the subjects who provided incomplete data in the PA questionnaire ($n = 130$), or who had not been tested for physical performance ($n = 70$). Furthermore, we excluded all potential subjects with notable comorbidities that could influence the frequency and degree of PA, that is, those who reported being incapable of walking 50 m independently ($n = 58$) and those with a history of arthritis ($n = 107$). Of the remaining 604 subjects, we further excluded those who reported a history of stroke ($n = 26$), coronary heart disease ($n = 61$), cancer ($n = 33$), and the one subject reporting cognitive dysfunction (Mini-Mental State Examination [MMSE] score <18) in the baseline survey. As a result of these exclusions, the final study population comprised 483 (231 male and 252 female) subjects. The mean age was 75.5 years (standard deviation [SD] = 4.2).

Data on medical care costs

We prospectively collected data on medical care use and costs for all individuals in the cohort study that extended from August 2002 to March 2008. We obtained the NHI claims history files from the Miyagi NHI Association. These files included the total number of outpatient visits, the total number of days of inpatient care, and the charges for outpatient and inpatient care, respectively.

When a beneficiary was withdrawn from the NHI, the date and reason were coded on an NHI withdrawal history file. This file identified the survival and emigration status for each subject. Both the NHI claims and withdrawal history files were linked with our baseline survey data file, with the beneficiary's ID number functioning as the key code. Monthly medical expenditures for each subject were calculated by dividing the total medical expenditures throughout the observation period by the number of months observed. We used monthly values rather than cumulative values to avoid underestimating medical expenditures for subjects who died or emigrated during the follow up.

Assessment of PA

A self-reported single-item questionnaire was used to estimate the different levels of PA in each subject. The subject was asked whether he or she had performed any activities from the following categories in the previous 12 months: walking, brisk walking, or sports (e.g. aerobics, tennis, swimming, jogging, etc.). If they had participated in a given activity, the frequency of and duration of time spent in performing the activity were ascertained using the following categories: for frequency

Table 1 Definition of physical activity level ($n = 483$)

	Low		Moderate		High	
No. of participants	115	90	114	46	66	52
Walking	None	Low	High	Any	Any	Any
Brisk walking	None	None	None	Low	High	Any
Sports	None	None	None	None	None	Low and high
Walking						
None	115	0	0	14	41	22
Low	0	90	0	15	1	14
High	0	0	114	17	24	16
Brisk walking						
None	115	90	114	0	0	32
Low	0	0	0	46	0	7
High	0	0	0	0	66	13
Sports						
None	115	90	114	46	66	0
Low	0	0	0	0	0	48
High	0	0	0	0	0	4

High, at least 3–4 times/week for at least 30 min each time; low, reporting some activity in the past year, but not enough to meet high levels; none, no physical activity.

(i) 1–2 times/month; (ii) 1–2 times/week; (iii) 3–4 times/week; or (iv) almost every day; and for duration (per walk or workout) (i) 0–30 min (<30 min); (ii) 0.5–1 h (≥0.5 h, <1 h); (iii) 1–2 h (≥1 h, <2 h); (iv) 2–3 h (≥2 h, <3 h); (v) 3–4 h (≥3 h, <4 h); or (vi) 4 h or more (≥4 h). Among the levels of exercise intensity, sports were considered the highest, followed in order by brisk walking and walking. Each of the three types was further classified into three subcategories according to the frequency and duration of the walks or workouts as follows:[19,20] (i) high, at least 3–4 times/week for at least 30 min each time; (ii) low, some activity in the past year, but not enough to meet the criteria for the high group; and (iii) none, no PA. Finally, we used these categories and subcategories to define the following three levels of PA (Table 1): (i) low, no sports, no brisk walking, low amount of walking; (ii) moderate, no sports, low amount of brisk walking, any amount of walking; and (iii) high, any amount of sports, any amount of brisk walking, any amount of walking. Table 1 also shows the number of participants according to the PA levels.

Assessment of physical performance measurement

Leg muscle power (w/kg)

Bilateral leg muscle power was measured on a horizontal leg extension apparatus (Combi Anaeropress 3500, Tokyo, Japan). Participants were positioned well back on a seat, supported at the waist by a belt, and their feet were placed on a sliding board with the knee joints angled at 90°. The resistance of the sliding board was adjusted according to the bodyweight. Participants were asked to extend their knees to push away the sliding board as hard as they could. The leg extension power was then measured. The trials were separated by 15-s rest intervals. The average of the two highest leg power measurements among five trials conducted was recorded as the "leg muscle power" and the resulting power was divided by the bodyweight.

Functional reach (cm)

Participants were asked to reach as far forward as possible while maintaining a fixed base of support, with their feet placed comfortably apart (approximately shoulder-width) but in symmetrical sagittal alignment. The distance reached was measured (in cm) on a tape measure fixed to the wall. This test was repeated three times and the longest distance measured was recorded.[21]

Timed "Up & Go" test (s)

Participants were seated in a free-standing padded armchair (46 cm high) and asked to rise (with or without using the armrests), walk to a mark 3 m away, turn around, walk back to the chair and sit down. The time between consecutive risings from the seat and contact made with the back of the seat was measured (s). This test was repeated three times and the fastest walk was recorded.[22]

10-m maximum walk test (m/s)

Each participant was asked to walk 10 m at his or her maximum walking speed. A stopwatch was used for timing the walk, and a counter was used to ascertain the number of steps. To eliminate the periods of acceleration and deceleration, subjects started their laps 3 m before the beginning of the walkway and concluded them 3 m beyond its end. The test was repeated three times, and the data of the fastest walk were recorded. These data were used to determine each subject's maximum walking speed (m/s).[23]

As regards the assessment of physical performance, the results of the four tests described above were each stratified into tertiles. We assigned, for each category of physical performance tests, a score of 3 for those in the highest tertile, 2 for those in the moderate and 1 for those in the lowest tertile. These scores were then added, so that they ranged 4–12. Those with scores in the ranges of 4–6, 7–9 or 10–12 were categorized as having a low, moderate or high level of physical performance, respectively.

Assessment of other variables

Anthropometric measures (e.g. height, bodyweight) were recorded by a standardized protocol. Blood pressure (BP) was measured at home with an HEM747IC device (Omron Life Science, Tokyo, Japan) that uses the cuff-oscillometric method to generate a digital display of systolic and diastolic pressures. The mean of 15.6 ± 10.5 (SD) BP measurements was used as the BP value. Participants who did not measure their home BP on at least 3 days were treated as having missing information on hypertension.

Blood samples were drawn from the antecubital vein of the seated subject with minimal tourniquet use. Specimens were collected in siliconized vacuum glass tubes containing sodium fluoride for blood glucose and no additives for lipid analyses.

The total cholesterol (T-C) and blood glucose levels of the subjects were measured by enzymatic methods (T-C, Denka Seiken, Tokyo, Japan; blood glucose, Shino-Test, Tokyo, Japan). Data on smoking status, alcohol consumption and history of liver or renal disease were obtained from the questionnaire survey. A well-trained pharmacist confirmed the drug information.

History of physical illness was evaluated on the basis of the responses ("yes" or "no") to questions concerning the history of liver and renal disease. Depressive symptoms were assessed according to the Japanese version of the 30-item Geriatric Depression Scale (GDS).[24] The participants were further tested for cognitive ability based on the MMSE.[25] Information on smoking (never, former and current smoking) and drinking (never, former and current drinking) status of the participants was obtained from a questionnaire survey.

Definitions of variables

Hypertension was defined as a home systolic BP reading of 135 mmHg or above and/or a home diastolic BP reading of 85 mmHg or above or use of antihypertensive agents.[26] Diabetes was defined as a casual blood glucose concentration of 200 mg/dL or above or the current use of antidiabetic medication. Hyperlipidemia was defined as a T-C level of 220 mg/dL or above, or the current use of a lipid-lowering agent. A GDS score of 14 or more or the use of an antidepressant was taken to indicate depressive symptoms.[27] An MMSE score of less than 24 was taken to indicate cognitive impairment.[28]

Medical care use and its costs were indicated by the number of hospital days, number of physician visits and medical care costs (total, inpatient and outpatient). Inpatient medical care costs included the cost of almost all the medical treatment received at hospitals, such as that incurred in diagnostic tests, medication, surgery, supplies and materials, paying the physician's fees and other personnel costs, but did not include hospital meal fees. Outpatient medical care costs included the money spent in medical treatment at outpatient clinics, prescribed drugs and home care services provided by physicians, but did not include dental care.

The number of hospital days, the number of physician visits and the medical care costs were calculated as per capita per month indices, including all subjects and months of observation irrespective of whether or not the former had received care.

Statistical analysis

Descriptive data are presented as means (95% confidence interval [CI]) or percentages. The variables' differences according to the levels of PA were examined by the ANCOVA for continuous variables or by the multiple logistic regression analysis for variables of proportion. The impact of PA or physical performance on the medical costs and number of outpatient visits and hospital days, respectively, were examined using ANCOVA after adjustment for age, sex, body mass index (BMI), hypertension, hyperlipidemia, diabetes mellitus, history of liver or renal disease, depressive symptoms, cognitive status, smoking and drinking habits/history, and physical performance score. All *P*-values for linear trends were calculated by using the applicable category of the PA levels (low, 1; moderate, 2; high, 3). The interactions between the PA and covariables were assessed by testing the interaction term added to the adjusted model as a covariate. The impact of PA on medical costs and the number of outpatient visits and hospital days was

Table 2 Baseline characteristics of subjects by levels of physical activity ($n = 483$)

	Physical activity levels			*P* for trend
	Low	Moderate	High	
No. of participants	205	160	118	–
Age (years)	76.0 (75.4–76.6)	75.6 (74.9–76.2)	74.4 (73.6–75.1)	<0.001
Sex (female)	61.0	48.1	42.4	<0.001
BMI (kg/m^2)	23.8 (23.3–24.2)	23.4 (22.9–23.9)	23.4 (22.8–23.9)	0.26
Hypertension	70.2	67.5	60.2	0.07
Hyperlipidemia	45.4	44.4	39.0	0.29
Diabetes	7.3	9.4	8.5	0.65
Impaired cognitive function (18 ≤ MMSE < 24)	8.8	6.9	8.5	0.84
Depressive symptoms (GDS ≥14 or use of antidepressant)	20.0	16.9	9.3	0.02
Smoking status				
Current smoker	17.1	12.5	11.9	0.16
Ex-smoker	23.4	38.5	39.0	<0.01
Non-smoker	56.7	47.5	49.2	0.14
Drinking status				
Current drinker	40.0	41.9	50.9	0.07
Ex-drinker	11.2	12.5	15.3	0.30
Non-drinker	44.4	39.4	31.4	0.02
Self-reported illness				
Renal	6.8	5.0	3.4	0.18
Liver	6.3	6.9	5.1	0.71
Physical performance				
Knee extension power (w/kg)	9.3 (8.8–9.9)	11.3 (10.7–11.9)	13.1 (12.3–13.8)	<0.0001
Functional reach (cm)	30.2 (29.5–31)	31.3 (30.4–32.1)	32.1 (31.1–33.2)	<0.01
Timed "Up & Go" test (s)	9.3 (9.1–9.5)	8.9 (8.7–9.1)	8.3 (8.1–8.6)	<0.0001
10-m maximum walking (m/s)	1.7 (1.6–1.7)	1.8 (1.7–1.8)	1.9 (1.9–2.0)	<0.0001
Log-transformed total physical performance score	1.9 (1.9–2.0)	2.0 (2.0–2.1)	2.2 (2.1–2.2)	<0.0001

Variables are presented as least squares mean (95% confidence interval) or %. BMI, body mass index; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination.

examined in association with physical performance levels after adjustment for the above mediator.

In this paper, monetary values were converted into \$US using the exchange rate of \$US 1.00 = 115 ¥. $P < 0.05$ was regarded as statistically significant. SAS software ver. 9.1 was used for all statistical calculations.

Results

Descriptive

Of the 483 subjects, 205 (42.4%) were categorized at the lowest level of PA, 160 (33.1%) at the moderate level and 118 (24.4%) at the highest level. Table 2 shows the baseline characteristics of subjects categorized by the PA level. The mean age was significantly lower at the highest PA level (*P* for trend <0.001). Although not statistically significant, the BMI was highest at the lowest PA level (*P* for trend = 0.26). Physical performance (including the results of the four tests and the total physical performance score) and PA were found to be positively associated (*P* for trend <0.01). Generally, participants with a higher PA had a better physical performance score. The proportion of subjects who were female, had depressive symptoms and were non-drinkers was significantly lower in the higher PA levels (*P* for trend <0.001, =0.02 and 0.02, respectively). Although the difference was not statistically significant (*P* for trend = 0.07), the proportion of subjects with hypertension was lowest at the highest PA level. In contrast, the proportion of ex-smokers was significantly higher at the higher PA levels (*P* for trend <0.01). Other than the above-mentioned, no significant difference was observed among the PA levels.

Table 3 Association between total medical care costs and physical performance levels (n = 483)

Physical performance	Physical performance levels Low	Moderate	High	P for trend[†]
Leg muscle power (w/kg)	0.8–8.7	8.8–12.6	12.7–23.4	–
No. of participants	160	162	161	–
Total medical costs, $US	892.4 (652.7–1132.2)[‡]	858.0 (631.2–1084.9)	718.2 (481.5–954.8)	0.01
Functional reach (cm)	6.3–29.1	29.2–33.5	33.6–45.6	–
No. of participants	159	161	163	–
Total medical costs, $US	847.5 (616.5–1078.4)	816.5 (583.6–1049.5)	806.1 (568.9–1043.2)	0.46
Timed "Up & Go" test (s)	16.8–9.4	9.4–8.1	8.1–5.6	–
No. of participants	161	162	160	–
Total medical costs, $	857.6 (626.9–1088.3)	819.8 (583.6–1056.0)	794.8 (561.4–1028.2)	0.25
10-m maximum walking (m/s)	0.9–1.6	1.7–1.9	1.9–3.1	–
No. of participants	160	162	161	–
Total medical costs, $US	898.6 (664.1–1133.0)	801.2 (572.1–1030.3)	795.5 (559.6–1031.5)	0.08
Total physical performance score	4–6	7–9	10–12	–
No. of participants	138	192	153	–
Total medical costs, $US	898.0 (662.0–1134.1)	823.4 (595.7–1051.1)	724.1 (485.1–963.2)	0.01

[†]Adjusted for age, sex, body mass index, hypertension, hyperlipidemia, diabetes, history of liver disease or renal disease, depressive symptoms, impaired cognitive function, smoking status, drinking status; [‡]Variables are presented as least-squares mean (95% confidence interval) (all such values).

Association between physical performance and PA or medical care costs per person

Table 3 shows the relationship between medical care costs and physical performance measurements. Levels of physical performance tests were stratified into tertiles. Although medical care costs tended to be higher in the poorer physical performance tertiles, the leg muscle power and total physical performance score were found to be the only statistically significant measures (P for trend = 0.01) among the four tests administered after adjustment for covariables. Although not statistically significant, the medical care costs were lowest in the highest 10-m maximum walking group (P for trend = 0.08).

Association between PA levels and medical care costs per person

Table 4 shows the adjusted association between the PA level and the medical care costs and the average number of days of hospital stay or visits. After adjustment for covariables, the significant inverse relation of PA levels with inpatient cost, average number of days of hospital stay and total cost was observed (P for trend = 0.02, 0.046, and 0.02, respectively). No significant interaction was observed between the physical performance score and PA levels for inpatient, outpatient or total medical care costs (data not shown). In contrast, no relation was found between the levels of PA and outpatient expenditures or average number of hospital visits in all models. Similar results were also observed when men and women were analyzed separately. No significant interaction was observed between the physical performance score and the sex of the patient regarding inpatient, outpatient or total medical care costs. Stratified association between the PA levels and the total medical care costs (least-squares mean, 95% CI) by physical performance levels after adjustment for variables in the full multivariate model in Table 4 are shown in Figure 1. Except for a small sample (n = 14) group characterized by high PA with lower physical performance, the PA was inversely associated with medical cost in all the physical performance categories.

Discussion

The main finding of this study was that higher PA levels were associated with lower medical care costs and hospitalization days among Japanese community-dwelling elderly individuals. Higher physical performance levels were also associated with lower medical care costs. However, the inverse association between PA and medical care costs persisted even after adjustment for the level of physical performance (P for interaction = 0.48). These results suggested that the beneficial effect of PA on medical cost might be consistently observed irrespective of their baseline physical performance.

The strength of our study lies in the fact that we have measured both the PA and the physical performance. The unique characteristics of the study enabled us to clarify whether the PA itself predicts the medical cost or whether it merely marks the physical performance.

Table 4 Association between physical activity levels and medical care costs ($n = 483$)

	Physical activity levels Low	Moderate	High	*P* for trend
No. of participants	205	160	118	–
Inpatient data, $US				
Model 1†	421.8 (227.4–616.1)‡	323.7 (123.4–524.0)	297.3 (90.0–504.5)	<0.01
Model 2§	389.3 (190.8–587.8)	296.7 (93.7–499.8)	282.3 (74.3–490.4)	0.02
No. of hospital days†				
Model 1†	1.9 (1.1–2.7)	1.5 (0.7–2.3)	1.4 (0.6–2.3)	0.02
Model 2§	1.7 (0.9–2.6)	1.4 (0.5–2.2)	1.4 (0.5–2.2)	0.046
Outpatient data, $US				
Model 1†	453.4 (346.6–560.3)	427.7 (317.6–537.9)	426.1 (312.2–540.1)	0.28
Model 2§	438.0 (328.9–547.2)	414.4 (302.7–526.0)	419.7 (305.3–534.0)	0.48
No. of physician visits†				
Model 1†	6.5 (4.6–8.4)	6.6 (4.6–8.5)	6.6 (4.5–8.6)	0.87
Model 2§	6.4 (4.4–8.3)	6.5 (4.4–8.5)	6.5 (4.4–8.6)	0.76
Total costs, $US				
Model 1†	875.2 (650.2–1100.2)	751.4 (519.5–983.4)	723.4 (483.4–963.4)	<0.01
Model 2§	827.3 (598.0–1056.7)	711.1 (476.4–945.8)	702.0 (461.6–942.4)	0.02

†Adjusted for age, sex, body mass index, hypertension, hyperlipidemia, diabetes, history of liver disease or renal disease, depressive symptoms, impaired cognitive function, smoking status, drinking status. ‡Variables are presented as least-squares mean (95% confidence interval) (all such values). §Adjusted for model 1 + total physical performance score.

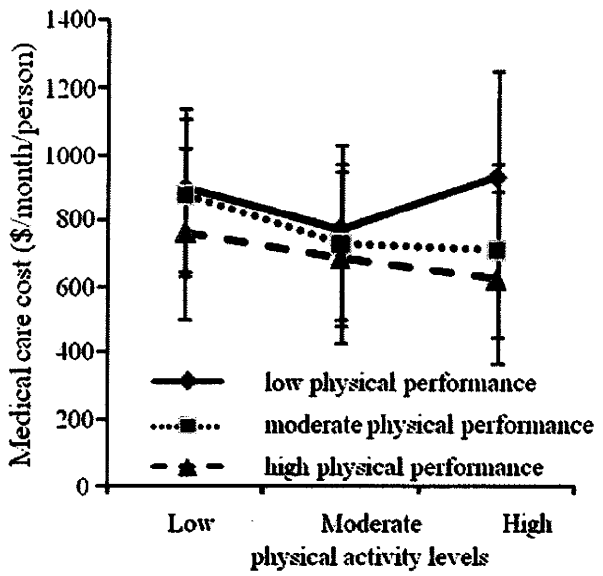

Figure 1 Association between physical activity levels and total medical care costs stratified by physical performance levels. Results from an analysis of covariance model adjusting for age, sex, body mass index, hypertension, hyperlipidemia, diabetes mellitus, history of liver disease or renal disease, depressive symptoms, impaired cognitive function, smoking status and drinking status. Variables indicate the adjusted least-squares mean. Error bars indicate 95% confidence intervals. Currency $US.

Individual reasons for medical treatment were not identified, but the fact that inpatient but not outpatient costs were higher among the community-dwelling subjects with lower levels of PA implies that these subjects may have suffered acute medical conditions requiring inpatient treatment. The outpatient care costs did not differ among the groups. The outpatient care costs were not influenced by the level of PA, partly because the proportion of elderly patients receiving medication for chronic diseases that did not affect their daily PA (e.g. hyperlipidemia or hypertension) did not differ among the groups, and such medication was mostly prescribed regularly for a long period of time. It should be noted that only one-fifth of the subjects in each group were not medicated.

As we have previously reported, it was found in a population study involving 27 431 Japanese men and women aged 40–79 years that those who walked for more than 1 h per day paid less for medical care.[10] We reported that both inpatient and outpatient costs taken cumulatively were smaller among the active walkers, which seems to conflict with our present result. This is probably because in the earlier study the population was younger and more than 70% of the participants reported that their health was good or excellent. Another factor responsible for the conflict in results might be the difference in the methods employed for estimating PA. Therefore, it is most likely that the majority of the previous study population was non-medicated and did not suffer from chronic diseases, which stands in remarkable contrast with the present study population. Wang *et al.* also reported in their cross-sectional study that the frequency of PA had a strong dose–response effect on health-care costs in those above the age of 65 years.[9] A 10-year follow up of the participants in a randomized clinical trial of walking in the USA revealed that the subjects in the walking group continued to walk longer and had lower hospitalization rates than those in the control group.[29] However, the physical performance of the participants was not evaluated in any of the previous studies.

By excluding the subjects with a history of stroke, cancer or coronary heart disease who potentially incur greater medical care costs than those without a similar history, the study population's selection bias was sufficiently minimized. The fact that the accumulated medical care cost during the initial 6 months did not differ among the groups shows that leading bias was minimized.

A stratified analysis by physical performance levels showed that the inverse dose–response relationship between total medical care costs and PA was observed in the moderate and high physical performance levels (Fig. 1). In the low physical performance level, the total medical care costs were highest at the highest PA level. Although we cannot validly explain this result, the number of subjects in the highest PA level was very small ($n = 14$), and therefore the mean medical care cost for that level would be imprecise.

This study has several limitations. First, because all the assessment were carried out in a public facility, the participants were sufficiently active and healthy to participate in the survey; therefore, it is possible that the current results would not be applicable to subjects at a higher risk. Moreover, because arthritis and remarkably low physical function might influence the frequency and degree of PA, and many diseases such as stroke, coronary heart disease and cancer can be a reason for large medical care cost at baseline, we also excluded these participants. Therefore, our results may not represent the general elderly population. However, we believe that these exclusions were necessary to investigate the relation of PA with medical care cost. Second, the diagnosis for each instance of medical care use was not available. This prevented an examination of the effects of exercise on particular diseases. Third, the intensity of walking, brisk walking and sports were not directly measured. Therefore, the proportional amount of PA in terms of the energy expenditure required for reducing medical care costs cannot be determined. However, because a person can easily discriminate his or her own "brisk walking" from ordinary walking,[30] it was suggested that the categorization of relative walking intensity based on the subjects' own perceptions was reliable.

In conclusion, this prospective study indicates that a higher level of PA was associated with lower medical care costs irrespective of physical performance among the elderly Japanese.

Acknowledgments

This study was supported by a Grant-in-Aid for Scientific Research (13557031) and by a Grant for Research Conducted by the Japanese Society for Promotion of Science (JSPS) (14010301) from the Ministry of Education, Culture, Sports, Science and Technology of Japan, by Research Grants (2002, 2003) from the Japan Atherosclerosis Prevention Fund, and by a Health Science Grant on Health Services (H16-seisaku-023) and a Grant for Comprehensive Research on Aging and Health (H16-choju-016) from the Ministry of Health, Labor and Welfare of Japan and by Health and Labor Science Research Grant from the Ministry of Health, Labor and Welfare Japan (H18-Choju-031).

References

1 Yu W, Ravelo A, Wagner TH *et al.* The relationships among age, chronic conditions, and healthcare costs. *Am J Manag Care* 2004; **10**: 909–916.
2 Morgan SG. Booming prescription drug expenditure: a population-based analysis of age dynamics. *Med Care* 2005; **43**: 996–1008.
3 Ministry of internal affairs and communications, statistics bureau: population census. [Cited 4 Oct 2007.] Available from URL: http://www.stat.go.jp/data/kokusei/topics/topics23.htm (In Japanese.)
4 Welfare And Medical Service NETwork System (WAM NET). [Cited 5 Oct 2007.] Available from URL: http://www.wam.go.jp/wamappl/bb13GS40.nsf/vcl/List?open (In Japanese.)
5 Sundquist K, Qvist J, Sundquist J *et al.* Frequent and occasional physical activity in the elderly: a 12-year follow-up study of mortality. *Am J Prev Med* 2004; **27**: 22–27.
6 Schroll M. Physical activity in an ageing population. *Scand J Med Sci Sports* 2003; **13**: 63–69.
7 Hu G, Jousilahti P, Barengo NC *et al.* Physical activity, cardiovascular risk factors, and mortality among Finnish adults with diabetes. *Diabetes Care* 2005; **28**: 799–805.
8 de Vreede PL, van Meeteren NL, Samson MM *et al.* The effect of functional tasks exercise and resistance exercise on health-related quality of life and physical activity. A randomised controlled trial. *Gerontology* 2007; **53**: 12–20.
9 Wang F, McDonald T, Reffitt B *et al.* BMI, physical activity, and health care utilization/costs among Medicare retirees. *Obes Res* 2005; **13**: 1450–1457.
10 Tsuji I, Takahashi K, Nishino Y *et al.* Impact of walking upon medical care expenditure in Japan: the Ohsaki Cohort Study. *Int J Epidemiol* 2003; **32**: 809–814.
11 Keeler EB, Manning WG, Newhouse JP *et al.* The external costs of a sedentary life-style. *Am J Public Health* 1989; **79**: 975–981.
12 Aoyagi Y, Park H, Watanabe E *et al.* Habitual physical activity and physical fitness in older Japanese adults: the Nakanojo Study. *Gerontology* 2009; **55**: 523–531.

13 Brach JS, FitzGerald S, Newman AB *et al.* Physical activity and functional status in community-dwelling older women: a 14-year prospective study. *Arch Intern Med* 2003; **163**: 2565–2571.

14 Brach JS, VanSwearingen JM, FitzGerald SJ *et al.* The relationship among physical activity, obesity, and physical function in community-dwelling older women. *Prev Med* 2004; **39**: 74–80.

15 Ringsberg KA, Gardsell P, Johnell O *et al.* The impact of long-term moderate physical activity on functional performance, bone mineral density and fracture incidence in elderly women. *Gerontology* 2001; **47**: 15–20.

16 Yamauchi J, Nakayama S, Ishii N. Effects of bodyweight-based exercise training on muscle functions of leg multi-joint movement in elderly individuals. *Geriatr Gerontol Int* 2009; **9**: 262–269.

17 Bocalini DS, Serra AJ, Murad N *et al.* Water- versus land-based exercise effects on physical fitness in older women. *Geriatr Gerontol Int* 2008; **8**: 265–271.

18 Niu K, Hozawa A, Guo H *et al.* Serum C-reactive protein even at very low (<1.0 mg/l) concentration is associated with physical performance in a community-based elderly population aged 70 years and over. *Gerontology* 2008; **54**: 260–267.

19 Pate RR, Pratt M, Blair SN *et al.* Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995; **273**: 402–407.

20 Niu K, Hozawa A, Fujita K *et al.* Influence of leisure-time physical activity on the relationship between C-reactive protein and hypertension in a community-based elderly population of Japan: the Tsurugaya project. *Hypertens Res* 2005; **28**: 747–754.

21 Duncan PW, Weiner DK, Chandler J *et al.* Functional reach: a new clinical measure of balance. *J Gerontol* 1990; **45**: M192–M197.

22 Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; **39**: 142–148.

23 Iwata M, Kondo I, Sato Y *et al.* An ankle-foot orthosis with inhibitor bar: effect on hemiplegic gait. *Arch Phys Med Rehabil* 2003; **84**: 924–927.

24 Niino N, Imaizumi T, Kawakami NA. Japanese translation of the Geriatric Depression Scale. *Clin Gerontol* 1991; **10**: 85–87.

25 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–198.

26 Chobanian AV, Bakris GL, Black HR *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; **289**: 2560–2572.

27 Brink T, Yesavage J, Lum O *et al.* Screening tests for geriatric depression. *Clin Gerontol* 1982; **1**: 37–44.

28 Siu AL. Screening for dementia and investigating its causes. *Ann Intern Med* 1991; **115**: 122–132.

29 Pereira MA, Kriska AM, Day RD *et al.* A randomized walking trial in postmenopausal women: Effects on physical activity and health 10 years later. *Arch Intern Med* 1998; **158**: 1695–1701.

30 Noble BJ. Clinical applications of perceived exertion. *Med Sci Sports Exerc* 1982; **14**: 406–411.

Original Article

Relationship between Peripheral Arterial Disease and Incident Disability among Elderly Japanese: the Tsurugaya Project

Akemi Nitta[1,2], Atsushi Hozawa[1,3], Shinichi Kuriyama[1], Naoki Nakaya[1,4], Kaori Ohmori-Matsuda[1], Toshimasa Sone[1], Masako Kakizaki[1], Satoru Ebihara[5], Masataka Ichiki[6], Hiroyuki Arai[2], and Ichiro Tsuji[1]

[1] Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan
[2] Department of Geriatrics and Gerontology Division of Brain Sciences Institute of Development, Aging and Cancer Tohoku University, Sendai, Japan
[3] Department of Public Health, Yamagata University Graduate School of Medical Science, Yamagata, Japan
[4] Department of Nutrition and Dietetics, Faculty of Family and Consumer Sciences, Kamakura Women's University, Kamakura, Japan
[5] Department of Internal Medicine and Rehabilitation Science Tohoku University Graduate School of Medicine, Sendai, Japan
[6] JR Sendai Hospital, Sendai, Japan

Aim: **The aim of this study was to investigate whether peripheral arterial disease (PAD) is predictive of disability and whether the relationship between PAD and disability can be fully explained by baseline physical functions.**

Methods: **We followed for five years 783 Japanese aged 70 years or older without a disability at baseline in 2003. We defined participants certificed as requiring long-term care as having incident disability. The hazard ratio (HR) and 95% confidence interval (95% CI) for incident disability were calculated using the Cox proportional hazards model.**

Results: **After adjusting for possible confounders other than physical function, the HR of incident disability among participants with PAD was 1.86 (95%CI: 1.06 to 3.26).**

Although the risk was attenuated (HR = 1.63, 95%CI: 0.92 to 2.86) after adding baseline physical function as a covariate, the HR was still high. Furthermore, the relation was not statistically significant, but the group with higher physical function and PAD also had a higher HR of incident disability than those who had higher physical function without PAD.

Conclusion: **PAD is an important predictor of disability even if the level of baseline physical function is high.**

J Atheroscler Thromb, 2010; 17:1290-1296.

Key words; peripheral arterial disease, incident disability, Japanese elderly prospective cohort study, long term care insurance certification

Introduction

The Aging of society is an important public concern in most countries[1]. The number of older people with disabilities will increase as the proportion of elderly in the population increases[2]. Therefore, it is important to establish ways of preventing as well as delaying the onset of disabilities.

To prevent incident disability, it is important to identify those at high risk. Peripheral arterial disease (PAD) is a risk factor for stroke and dementia[3-5], both of which in turn are important risk factors for disability[6]. Furthermore, individuals with PAD are known to have reduced physical function[7-9]. Thus, PAD might

Corresponding author: Akemi Nitta, MSc, Institute of Development, Aging and Cancer, Tohoku University, Department of Geriatrics and Gerontology, 4-1 Seiryo-machi, Aoba-ku, Sendai, 980-8575, JAPAN
TEL: +81-22-717-7182 FAX: +81-22-717-8498
E-mail: akemin0125@yahoo.co.jp
Received: April 12, 2010
Accepted for publication: July 29, 2010

be an important predictor of incident disability. However, only a few studies have investigated the relationship between PAD and disability[7-9]. Furthermore, only one study has investigated the relationship between PAD and future mobility loss with reference to baseline physical function[9]. Therefore, there is little evidence to suggest whether PAD can be used to predict disability or whether the relationship between PAD and disability can be fully explained by baseline physical function. The present study was conducted with the aim of clarifying these issues.

Methods

Study participants

The Tsurugaya project was a comprehensive geriatric assessment, which included medical status, physical function and cognitive function, performed in 2002 and 2003[10-15].

In this study, we used the data for 2003 because baseline disability status as assessed by long-term care insurance (LTCI) certification was available.

Among 2925 individuals aged 70 years and older living in the Tsurugaya area of Sendai, containing the largest cities in the Tohoku area of Northern Japan, 924 gave informed consent both to participate in the study and for the follow-up of their LTCI status.

Among the 924 participants, we excluded those whose ankle brachial index (ABI) had not been measured ($n=1$), who had already been certificated as having a disability as assessed by the LTCI certification at baseline ($n=82$), and who had not undergone a measurement of physical function ($n=58$). As a result of these exclusions, we followed 783 participants in this study.

The study protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine.

Measurements

ABI Measurement

Bilateral ABI was measured in all participants using a FORM ABI/PWV device (Colin Co., Komaki, Japan), which incorporates an automatic oscillometer[10].

The FORM ABI/PWV has four cuffs that can measure blood pressure (BP) levels simultaneously in both arms and both legs, and automatically calculates the ABI[10].

This device is useful for mass medical examinations and population-based studies because it enables measurements of ABI and brachial ankle pulse wave velocity in a short time and is not affected by operator technique[10]. Validation of this device has been reported[16]. This device was also used in several epidemiological studies[10, 17, 18].

We defined participants with an ABI of ≤ 0.90 at either leg as having PAD[10, 19].

Physical function parameters

Physical function was measured using four tests: knee strength extensions, functional reach, the "Ten-meter maximum walk test" and the "timed up and go" test.

These functional tests were performed by a well trained physical therapist as described below[12, 20].

Knee strength extensions

The participants were placed well back on a seat, and the waist was fixed with a belt. The knee joint was angled at 90°. Isometric contractions lasting 5 s each were conducted separated by 15-s rest intervals. Peak power was detected, calculated, and recorded in watts by a microcomputer. The average of the two highest measurements among 5 trials was recorded as isometric strength performance. To measure this function, we used an Aneropress 3500 (Combi Wellness, Tokyo).

To minimize differences in body mass, leg extension power was expressed as the average peak of the leg relative to body weight (W/kg)[12].

Functional reach

We also measured how far an individual can reach forward beyond arm's length while maintaining a fixed base of support in a standing position, without losing balance. We attempted the test twice and adopted the higher of the two scores[20].

Ten-meter maximum walk test

Each participant was asked to walk 10 m at maximum speed. A stopwatch was used for timing, and a counter was used to obtain the number of steps. To eliminate periods of acceleration and deceleration, the participants started walking 3 m before entering the walkway and stopped walking 3 m beyond its end. The test was repeated three times, and the data for the fastest walk were recorded[12].

"Timed up and go" test

The participants were seated in a free-standing padded armchair (46 cm high) and asked to rise (with or without using the arm rests), walk to a mark 3 m away, turn around, and walk back to the chair and sit down. The time between rising from the seat and making contact with the back of the seat was measured in seconds. This test was repeated three times and the time of the fastest trial was recorded[12].

Other measurements

Information on smoking status, history of diseases and physical activity was obtained using questionnairea. Drug information was confirmed by an experienced pharmacist[12].

Casual BP was measured using an automated device (HEM747IC: Omron Life Science Co., Ltd., Tokyo, Japan)[10]. BP was measured at screening under resting conditions. Participants were considered to be hypertensive if their systolic BP was at least 140 mmHg or diastolic BP was at least 90 mmHg, or if they were taking antihypertensive agents. Participants were considered to have a high blood glucose concentration if their casual (non-fasting) blood glucose level was at least 7.77 mmol/L, or if they used antidiabetic medication[10, 21]. With regard to physical activity, we obtained information on the frequency and duration of walking, brisk walking and sports by self-reported questionnaire. Based on this information, we defined 6 levels of physical activity as described in our previous report[13]. Physical activity was assessed as leisure time physical activity. We classified into three subcategories according to the frequency and duration of walks or workouts as follows.1) High, 3 of more times per week for at least 30 min each time. 2) Low, some activity in the past year, but not enough to meet the criteria for the high group; and 3) None, no LTPA. Finally, we used these categories and subcategories to define the following six levels of LTPA 1) Level 1, no sports, no brisk walking, no walking; 2) Level 2, no sports, no brisk walking, low amount of walking; 3) Level 3, no sports, no brisk walking, high amount of walking; 4) Level 4, no sports, low amount of brisk walking, any amount of walking; 5) Level 5, no sports, high amount of brisk walking, any amount of walking; 6) Level 6, any amount of sports, any amount of brisk walking, any amount of walking. We defined higher physical activity levels as at least brisk walking (Level 4-6) in this study.

Outcome measurement

Long-term care insurance certification

Incident disability was assessed by LTCI certification. The LTCI system was launched as part of the national insurance system in April 2000[22-24]. We followed up incident disability for five years.

In Japan, people aged 40-64 years who are diagnosed with aging-related diseases (e.g. Alzheimer's disease and stroke) and those aged ≧65 years who are certified as requiring care are eligible for benefits based on level of care under the LTCI system[1]. To receive LTCI services, an elderly person or his/her caregiver (family or professional) must contact the municipal government to have the applicant's care needs officially certified[23]. A trained local government official visits the applicant's home to evaluate nursing care needs using a questionnaire assessing current physical and mental status and use of medical procedures[23]. These results are entered into a computer to calculate the applicant's standardized scores for physical and mental functions, estimate the amount of time required for care for the nine categories (grooming/bathing, eating, using the toilet, transferring, eating, assistance with instrumental activities of daily living, behavioral problems, rehabilitation, and medical services)[23]. Based on the nationally determined system, it is decided whether the applicant deserves to be certified as eligible for LTCI services and the system assigns a care-needs level determined by a confirmed certification board consisting of physicians, nurses and other experts in health and social services appointed by the local mayor.

The care-needs level consists of 7 levels which are well correlated with the Barthel Index (Spearman's coefficient: −0.86) and the Mini-Mental State Examination (Spearman's coefficient: −0.42)[24].

The definition is considered a comprehensive measure of disability in the elderly[25].

We asked the Sendai city municipal authority to provide information on LTCI certification including care level and date of certification, annually up until June 30th, 2008 (for 5 years).

Statistical analysis

Baseline characteristics were compared by the χ^2 test and t-test, as appropriate (**Table 1**). The hazard ratio (HR) and 95% confidence interval (95%CI) for the relationship between PAD and incident disability was calculated using a Cox proportional hazards model (**Table 2**). We censored participants who died or moved away during follow-up. We also analyzed the relationship between PAD and composite outcome of disability or mortality.

For the Cox proportional hazards modeling, we used an age-sex adjusted model (Model 1); a multiple adjustment model adjusted for smoking status, hypertension, high blood glucose level, history of stroke and physical activity (Model 2); and a third model to confirm the effect of lower physical function in PAD participants on the relationship between PAD and disability, with baseline values of all physical functional

Table 1. Baseline Characteristics of Participants, the Tsurugaya Project, 2003.

	With PAD $n=36$	Without PAD $n=747$	p-value
Age (year)	77.6±4.8	75.5±4.4	<0.01
Sex (% : male)	69.4	48.7	0.02
Smoking status (%)			
Current smokers (%)	25.0	10.4	<0.01
Past smokers (%)	44.4	33.2	
Never smokers (%)	30.6	56.4	
Hypertension (%)	86.1	73.1	0.08
High blood glucose (%)	36.1	17.5	<0.01
History of stroke (%)	13.9	2.8	<0.01
Physical activity (%)	19.4	35.3	0.05
Functional measures			
Knee strength extension (W/Kg)	7.5±4.4	8.8±4.4	0.07
Functional reach (cm)	28.3±6.5	29.5±5.5	0.22
Ten-meter maximum walk test(m/s)	1.6±0.4	1.8±0.3	<0.01
Timed up and go test (s)	10.3±2.6	9.0±1.7	<0.01

Variables are presented as the mean ±Standard Deviation (SD) Physical activity: brisk walking or sports more than 3 times/week.

Table 2. Hazard Ratio for Incident Disability and Incident Disability or Mortality among participants with PAD and without PAD, the Tsurugaya Project, 2003-2008.

Endpoint	Disability		Disability and/or mortality	
	Without PAD	With PAD	Without PAD	With PAD
Number of Participants	747	36	747	36
Number of Events	140	15	169	19
Hazard Ratio (95% Confidence Interval)				
Model 1	1.00	2.12 (1.22-3.69)	1.00	2.18 (1.33-3.56)
Model 2	1.00	1.86 (1.06-3.26)	1.00	1.84 (1.12-3.04)
Model 3	1.00	1.63 (0.92-2.86)	1.00	1.67 (1.01-2.76)

Model 1: age and sex.
Model 2: Model 1 + smoking status, hypertension, high blood glucose, history of stroke and physical activity.
Model 3: Model 2 + physical functions.

measures as confounding factors (Model 3). To adjust for physical function, we assigned each function a score of 1 to 4 according to the sex-specific physical function quartile and added these scores as covariates (continuous). To assess whether PAD is predictive of disability independent of physical function, we conducted a combination analysis. To create a combined category, we used the median value of physical function as the cut-off. As a result, four combined categories were established, i.e. high physical function without PAD, high physical function with PAD, low physical function without PAD and low physical function with PAD. In these analyses, we used the group with high physical function without PAD as a reference.

The level of statistical significance was set at $p<0.05$. All statistical analyses were performed with SAS software, version 9.1 (SAS Institute, Cary, USA).

Results

Table 1 shows baseline characteristics according to the presence or absence of PAD.

Mean age was significantly higher in participants with PAD than those without PAD.

The proportions of men, current and past smokers, and subjects with hypertension, high blood glucose levels and stroke also were significantly higher among the participants with PAD than those without

Table 3. Hazard Ratio for the Incident Disability for Participants with and without PAD According to categories of Physical Function Defined for the Tsurugaya Project, 2003-2008.

Function Level	With PAD		Without PAD	
	Low	High	Low	High
(a) Knee strength extension				
Number	27	9	358	389
Event	13	2	97	43
Hazard Ratio (95% Confidence Interval)	2.99 (1.51-5.92)	1.86 (0.45-7.77)	1.68 (1.14-2.47)	1.00
(b) Functional reach				
Number	22	14	366	381
Event	13	2	94	46
Hazard Ratio (95% Confidence Interval)	3.60 (1.84-7.08)	0.93 (0.22-3.88)	1.57 (1.08-2.28)	1.00
(c) Ten-meter maximum walk test				
Number	19	17	262	485
Event	10	5	84	56
Hazard Ratio (95% Confidence Interval)	3.13 (1.50-6.51)	2.27 (0.89-5.77)	2.03 (1.41-2.93)	1.00
(d) Timed up and go test				
Number	24	12	372	375
Event	12	3	96	44
Hazard Ratio (95% Confidence Interval)	2.96 (1.48-5.90)	2.20 (0.67-7.22)	1.72 (1.18-2.49)	1.00

PAD. Physical functions were consistently worse in participants with PAD, the difference being statistically significant for the timed up and go test and ten-meter maximum walk test.

Table 2 shows the relationship between PAD and incident disability. During the five years of follow-up, among 783 participants, 33 died, and 7 transferred. We observed 155 incident disability cases during the follow-up period. Compared with participants without PAD, the age-sex adjusted HR for incident disability was 2.12 (95%CI: 1.22 to 3.69) in participants with PAD, model 1. After adjustments for further possible confounding factors, the HR for incident disability among participants with PAD was 1.86 (95%CI: 1.06 to 3.26) in model 2. Because physical function might be a symptom of PAD, we considered Model 2 to be the most important for estimating the relation between PAD and incident disability. After additional adjustments for physical functions, the HR for incident disability among participants with PAD was 1.63 (95%CI: 0.92 to 2.86) in model 3.

When we used composite outcome of disability or mortality, the results in Models 1, 2 and 3 were 2.18 (95%CI: 1.33 to 3.56), 1.84 (95%CI: 1.12 to 3.04), and 1.67 (95% CI: 1.01 to 2.76), respectively.

Table 3 shows the HR for incident disability using a combination of PAD status and physical function status. For every baseline physical function, the HR for incident disability was highest among PAD patients with low physical function, and the increase in risk was statistically significant. Although not statistically significant, the HR for disability tended to be higher among participants with high physical function with PAD than participants with high physical function without PAD, except for functional reach.

Discussion

The present study demonstrated that the participants with PAD had an increased risk of disability compared with the participants without PAD. Because adjustments for baseline physical function attenuated this relationship, the poorer physical function in PAD patients played an important role in incident disability. However, the risk was still high even after the adjustments for baseline physical function, and PAD patients with higher physical function also had a higher risk of incident disability. Thus, the relationship between PAD and disability was not fully explained by baseline physical function.

Our study had several strengths. First, it measured both ABI and several physical functions such as muscle strength, balance and velocity of walking. Thus, we were able to assess whether PAD is predictive of disability independent of these physical functions. This paper is the second to have investigated the association of PAD with disabilities including an adjustment for baseline physical function. Second, we