## 学位論文内容の要旨 (Summary of dissertation)

博士の専攻分野の名称 博士 (医学) (Degree conferred: Doctor of Philosophy) 氏名 趙文静 (Name of recipient: WENJING ZHAO)

学位論文題名

(Title of dissertation)

Gait speed, daily walking and all-cause mortality in the younger-elderly Japanese: a cohort study (日本の前期高齢者における歩行速度、日常的な歩行習慣とその後の死亡:コホート研究から)

Background & Objective: Average life expectancy is still keeping rising almost linearly, with no sign of deceleration, especially in more developed countries, where it was estimated to increase to 78 years by 2010-2015, and 83 years by 2045-2050. In the past 60 decades, the average life expectancy in Japan also had been increased linearly, though the afterward trend was in a slower rise. Although the growth of the elderly was slow after 2007, the proportion of aging population will be 33.4% in 2035, and is projected up to 39.9% in 2060. In particularly, the older-elderly (≥75 years) is increasing more rapidly than does the younger-counterpart (65-74 years). The global and national evidence have shown substantial reductions in disability among the ageing population, however, physically and psychologically functional declines were prevalent along with diminishing mortality and increasing life expectancy, particularly in Japan, the country with the oldest population through the world. Maintenance of physical and psychological functioning is the foundation of keeping the elderly people independently carrying out the activities of daily living. A range of common instruments were applied for screening functional declines, and gait speed has been considered as a simple, safe, accessible, and sensitive instrument to identify the older population at high risk of functional declines and the subsequent adverse outcomes. It is reported that functional declines in the early stage can be reserved through targeted intervention, such as physical activity. One of the priorities of successful aging is to identify people at high risk of functional declines and apply the targeted strategy to delay the adverse outcomes caused by functional declines. In the Western countries, previous studies have demonstrated the association between gait speed and mortality among the older population, but few studies took physical activity into account. Meanwhile, no study in this regard in Japan is conducted. In this context, two relevant study were conducted that study one focused on the association between gait speed and all-cause mortality in younger-elderly Japanese and determined whether daily walking modifies this association; based on the results obtained in the study one, study two was designed to explore the health benefits of daily walking on all-cause mortality in the younger elderly men with or without major critical diseases (heart diseases, cerebrovascular diseases, or cancer).

**Study 1: [Objective]** To investigate the influence of gait speed on mortality among younger-elderly Japanese and determine whether daily walking modifies that association. **[Participants & Methods]** The data came from the New Integrated Suburban Seniority Investigation Project (the NISSIN Project) —an ongoing age-specific prospective cohort study. Of totally 3073 community-dwelling residents (1548 men, 1525 women) who were 64 years old at the beginning of the given survey year and agreed to register as cohort members from 1996 through 2005, 2105 participants (990 men and 1025 women) were used in the final analyses after excluding the subjects who entered the study after

2003 (617 people), those who reported a history of heart disease, cerebrovascular disease, or cancer (437 people) and those lacking data on gait speed (four people). Cox proportional-hazard regression was applied to estimate the hazard ratios (HRs) for all-cause mortality during 10 years and 95% confidence intervals (CIs). **[Results]** Slow gait speed was significantly associated with increased all-cause mortality among men after full adjustment (HR, 1.72; 95% CI, 1.08–2.63). This association disappeared when men with slow gait speed walked  $\geq$ 1h/d (HR, 0.98; 95% CI, 0.34–2.25) compared with subjects with normal or fast gait speed walking >1h/d. Slow gait speed yielded a threefold greater risk of mortality when women walked  $\geq$ 1h/d (HR, 3.04; 95% CI, 1.34–6.49), compared with the reference group. **[Discussion]** The association between slow gait speed and mortality among younger-elderly subjects living in communities was consistent with previous studies, which have demonstrated the association among the participants aged  $\geq$ 65,  $\geq$ 75, and even  $\geq$  85 years. Daily walking could be considered an effective modifiable factor in the association between gait speed and mortality among mortality among men.

Study 2: [Objective] To investigate health benefits of daily walking on mortality among younger-elderly men with or without major critical diseases. [Participants & Methods] The data came from the NISSIN Project. A total of 1239 men were selected as the study sample after excluding those who entered the study after 2003 (304 subjects), and men with missing data on daily walking (5 subjects). The method was the same to that in Study one. **[Results]** For men without critical diseases, mortality risk declined linearly with increased walking time after adjustment for confounders (P trend=0.009). Walking  $\geq 2$  hours/day was significantly associated with lower all-cause mortality (HR: 0.49, 95% CI: 0.28-0.80). For men with critical diseases, walking 1-2 hours/day showed a significant protective effect on mortality compared with walking <1 hour/day after adjustment for confounders (HR: 0.30, 95% CI: 0.08–0.91). [Discussion] A linear association between daily walking and all-cause mortality among men without major critical diseases was detected, which was consistent with the few existing reports that mortality from cardiovascular diseases, cancer, or all-causes among older men was decreased with increasing walking distance or duration. However, there was a peak in benefit at an intermediate level of daily walking for men with major critical diseases. The precise mechanism to explain why long duration of physical activity confers no additional benefits for the elderly is still unclear. An intermediate walking duration might be an optimal amount of time for men with major critical diseases owing to the heterogeneity of physical fitness. This amount of time might appropriate for their capacity to undertake physical activities, while any longer is unlikely to yield any benefits.

**Limitations:** First, self-reported gait speed and daily walking time could be the main limitation of the present study. Second, the sample size for men with major critical diseases was small compared with previous analogous studies that involved physical activity in patients with established cardiovascular diseases or cancer.

**Conclusions:** Slow gait speed was associated with increased mortality among the younger-elderly Japanese, and daily walking could modify this association among men. Walking longer period was associated with decreased mortality among the younger-elderly men without heart diseases, cerebrovascular diseases or cancer, which help understand the path of how daily walking modifies the association between gait speed and mortality among men.

**Future study:** To determine whether daily walking could contribute to improvement of functional capacity or at least maintenance of functional capacity. Meta-analysis might be conducted to conclude the previous evidence that whether or how much of physical activity is beneficial for the frail or venerable older people suffering from different chronic conditions.