Sari Stenholm

Obesity as a Risk Factor for Walking Limitation in Older Finnish Men and Women

Mediating Factors, Long-Term Risk and Coexisting Conditions

Publications of the National Public Health Institute A 10/2007

Department of Health and Functional Capacity,
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MEDIATING FACTORS, LONG-TERM RISK AND COEXISTING CONDITIONS

ACADEMIC DISSERTATION

To be presented with the permission of the Faculty of Sport and Health Sciences of the University of Jyväskylä for public examination in the Auditorium of the Rehabilitation Center Petrea, on August 17, 2007 at 12 o´clock noon.

Department of Health and Functional Capacity,
National Public Health Institute, Turku, Finland
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Publications of the National Public Health Institute
KTL A10 / 2007

Julkaisija-Utgivare-Publisher

Kansanterveyslaitos (KTL)
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ISBN 978-951-740-700-7
ISSN 0359-3584
ISBN 978-951-740-701-4 (pdf)
ISSN 1458-6290 (pdf)

Kannen kuva - cover photographic: Pekka Stenholm

Edita Prima Oy
Helsinki 2007

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I enjoy talking with very old people. They have gone before us on a road by which we, too, may have to travel, and I think we do well to learn from them what it is like.

- Socrates, in Plato's *The Republic*

Sari Stenholm, Obesity as a risk factor for walking limitation in older Finnish men
and women. Mediating factors, long-term risk and coexisting conditions.
Publications of the National Public Health Institute, A10/2007, 94 Pages
ISBN 978-951-740-700-7; 978-951-740-701-4 (pdf-version)
ISSN 0359-3584; 1458-6290 (pdf-version)
http://www.ktl.fi/portal/4043

ABSTRACT

Walking is a critical component in maintaining independent and high quality of life in old age, and difficulties in walking often precede more severe disability. Obesity is a known risk factor for several diseases, but a limited number of studies have examined the negative effect of obesity on walking or general mobility. Moreover, relatively little is known about the possible mechanisms through which obesity affects walking performance. This study was conducted to explore obesity as a risk factor for walking limitation, and to examine the role of different diseases and biological indicators in that association. Furthermore, obesity and physical impairments were studied as long-term risk factors in predicting limitations in later life walking.

This study targeted Finnish men and women aged 55 years or older, and it was based on the nationwide cross-sectional population-based Health 2000 Survey (n = 3 392) and the prospective Mini-Finland Follow-up Survey with a 22-year follow-up (n = 1 278). Walking limitation was defined as measured maximal walking speed less than 1.2 m/s, supplemented with self-reported difficulty in walking 500 meters for those who did not take part in the walking speed test. In the health examination of the Health 2000 Survey, body composition, body mass index, waist circumference, and handgrip strength were measured, medical conditions were diagnosed by a physician, and a blood sample was drawn. Recalled height at the age of 20 years and recalled weight at the ages of 20, 30, 40 and 50 years were recorded. At the baseline of the Mini-Finland Follow-up Survey, body mass index, handgrip strength and ability to squat were measured, and ability to run 500 meters was elicited. The main statistical method used in this study was logistic regression analysis.

In the cross-sectional setting, overweight and obesity were independently associated with walking limitation, more strongly in women than in men. Type 2 diabetes in men and knee osteoarthritis in women were the diseases which contributed most to the association between obesity and walking limitation. In addition, increased C-reactive protein level and low handgrip strength were found to mediate the association between high body fat percentage and walking limitation. The 22-year follow-up study showed that high body mass index and physical impairments measured at middle-age predicted walking limitation in later life. Based on a retrospective design, obesity duration over several decades increased the risk of walking limitation. Finally, overweight or obese persons with coexisting diseases or physical impairments had a high risk of current or future walking limitation compared with the risk associated with excess body weight alone.

The findings of this study show that obesity and obesity duration throughout the lifespan as well as obesity and coexisting conditions are important risk factors influencing walking in older person. The results of the present study may be useful when planning and targeting efficient interventions to prevent and alleviate walking limitation in older people. Future research using prospective and experimental settings is needed to confirm the role of diseases, low-grade inflammation, and decreased muscle strength in the pathway from obesity to walking limitation.

Keywords: body composition, coimpairment, comorbidity, epidemiological studies, inflammation, mobility, muscle strength, obesity, older people, walking

Sari Stenholm, Lihavuus kävelyvaikeuksien riskitekijänä ikääntyvillä suomalaisilla miehillä ja naisilla. Mekanismit, pitkäaikaiset vaikutukset sekä sairauksien ja fyysisen suorituskyvyn merkitys.
Kansanterveyslaitoksen julkaisuja, A10/2007, 94 sivua
ISBN 978-951-740-700-7; 978-951-740-701-4 (pdf-versio)
ISSN 0359-3584; 1458-6290 (pdf-versio)
http://www.ktl.fi/portal/4043

TIIVISTELMÄ

Kävelykyky vaikuttaa olennaisesti ikääntyvän ihmisen elämänlaatuun ja hänen edellytyksiinsä selviytyä ilman muiden apua. Usein kävelyvaikeudet ennustavat vielä vaikeampien toiminnanvajavuuksien ilmaantumista. Lihavuus on monien sairauksien tunnettu riskitekijä, mutta lihavuuden kielteisiä vaikutuksia kävelykykyyn on tutkittu vähän. Tietoa on niukasti myös niistä mekanismeista, joiden välityksellä lihavuus rajoittaa kävelykykyä. Tässä tutkimuksessa tarkasteltiin lihavuutta kävelyvaikeuksien riskitekijänä ja samalla myös erilaisten biologisten tekijöiden ja kroonisten sairauksien osuutta lihavuuden ja kävelyvaikeuksien väliseen yhteyteen. Lisäksi tutkittiin miten keski-iällä todettu lihavuus ja heikentynyt fyysinen suorituskyky ennustavat kävelyvaikeuksien ilmaantumista myöhemmällä iällä.

Tutkimuksen kohdejoukkona olivat 55 vuotta täyttäneet suomalaiset miehet ja naiset. Tutkimus perustui suomalaista aikuisväestöä edustavaan Terveys 2000 -tutkimukseen (n = 3 392) sekä sen yhteydessä tehtyyn seurantatutkimukseen (n = 1 278), jossa tutkittiin 22 vuotta aikaisemmin Mini-Suomi -tutkimukseen osallistuneita henkilöitä. Tutkittavan kävelyn katsottiin olevan vaikeutunutta, jos hänen maksimaalinen kävelynopeutensa oli alle 1.2 m/s tai mikäli tutkittava ei osallistunut kävelynopeustestiin, hän ilmoitti vaikeuksia 500 metrin kävelyssä. Terveys 2000 -tutkimuksessa mitattiin kehon koostumus, painoindeksi, vyötärönympärys ja käden puristusvoima. Lisäksi lääkäri diagnosoi tutkittavan sairaudet kliinisen tutkimuksen perusteella ja häneltä otettiin verinäyte. Tutkittavalta kysyttiin myös hänen pituuttaan 20 vuoden iässä ja painoa 20-, 30-, 40- ja 50-vuotiaana. Mini-Suomi -tutkimuksen lähtötilanteessa mitattiin painoindeksi, käden puristusvoima ja kyykistymiskyky sekä tiedusteltiin tutkittavan suoriutumista 500 metrin juoksemisesta. Pääasiallisena tilastomenetelmänä tutkimuksessa käytettiin logistista regressioanalyysia.

Poikkileikkausasetelmassa ylipainon ja lihavuuden havaittiin olevan itsenäisesti yhteydessä kävelyvaikeuksiin, selvemmin naisilla kuin miehillä. Kroonisista sairauksista lihavuuden ja kävelyvaikeuksien välistä yhteyttä selittivät parhaiten miehillä tyypin 2 diabetes ja naisilla polvinivelrikko. C-reaktiivisen proteiinin kohonneen pitoisuuden ja käden puristusvoiman heikkouden todettiin vastaavasti välittävän kehon korkean rasvaprosentin ja kävelyvaikeuksien välistä yhteyttä. 22 vuoden seurannassa keski-iällä todetun korkean painoindeksin ja huonon fyysisen suorituskyvyn havaittiin ennustavan kävelyvaikeuksien ilmaantumista myöhemmällä iällä. Retrospektiivisessä tarkastelussa ilmeni, että pitkään jatkunut lihavuus lisäsi kävelyvaikeuksien riskiä. Kävelyvaikeuksien riski oli selvästi suurempi niillä ylipainoisilla ja lihavilla henkilöillä, joilla oli samanaikaisia sairauksia tai fyysisen suorituskyvyn heikkouksia verrattuna niihin, joilla ei sellaisia ollut.

Tämän edustavaan väestöaineistoon perustuvan tutkimuksen tulokset osoittavat, että tutkimushetkellä havaittu ja pitkään kestänyt lihavuus sekä sen ohessa samanaikaisesti esiintyvät krooniset tilat ovat merkittäviä ikääntyvien henkilöiden liikkumiskyvyn riskitekijöitä. Tutkimuksen tulokset voivat palvella ikääntyvien ihmisten kävelyrajoitusten ennaltaehkäisyyn ja lieventämiseen suunnattujen interventioiden suunnittelua. Kroonisten sairauksien, lieväasteisen tulehduksen ja heikon lihasvoiman merkitys lihavuuden ja kävelyvaikeuksien välisen yhteyden selittäjinä on syytä vielä varmistaa uusilla pitkittäisaineistoihin ja kokeellisiin tutkimusasetelmiin perustuvilla lisätutkimuksilla.

Avainsanat: epidemiologiset tutkimukset, fyysinen kunto, ikääntyneet, inflammaatio, kehon koostumus, kävely, lihasvoima, lihavuus, liikkumiskyky, moniongelmaisuus, monisairastavuus

CONTENTS

ABBREVIATIONS

ADL	Activities of daily living
BIA	Bioelectric impedance analysis
BMI	Body mass index
CI	Confidence interval
CRP	C-reactive protein
CT	Computed tomography
CV	Coefficient of variation
DXA	Dual energy X-ray absorptiometry
ICC	Intra-class correlation
IL-6	Interleukin-6
MRI	Magnetic resonance imaging
OR	Odds ratio
r	Pearson correlation coefficient
ROC	Receiver operator characteristics
SD	Standard deviation
TNF-α	Tumor necrosis factor-α
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original articles referred to in the text by their Roman numerals:

I Stenholm S, Sainio P, Rantanen T, Alanen E, Koskinen S. The Effect of Co-morbidity on the Association of High Body Mass Index with Walking Limitation among Men and Women aged 55 years and older. *Aging Clin Exp Res*. 2007; 19(4): 000–000. In press.

II Stenholm S, Rantanen T, Heliövaara M, Koskinen S. The mediating role of C-reactive protein and handgrip strength between obesity and walking limitation. *J Am Geriatr Soc*. In press.

III Stenholm S, Rantanen T, Alanen E, Reunanen A, Sainio P, Koskinen S. Obesity History as a Predictor of Walking Limitation at Old Age. *Obesity.* 2007; 15(4): 929–938.

IV Stenholm S, Sainio P, Rantanen T, Koskinen S, Jula A, Heliövaara M, Aromaa A. High Body Mass Index and physical impairments as predictors of walking limitation 22 years later in adult Finns. *J Gerontol A Biol Sci Med Sci*. 2007; 62A(7): 000–000. In press.

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1 INTRODUCTION

The “graying of Finland” is proceeding at a rapid pace. The current population projection suggests that the proportion of people aged 55 years or older will rice from 30% in year 2005 to 39% in 2040 (Statistics Finland 2006). Relatively similar trends are expected in other European countries, as well (Nieminen and Koskinen 2006). Despite the fact that older adults are healthier today than ever before (Aromaa et al. 2006), with advancing age the possibility of diseases, impairments, limitations, and disabilities increases. One of the most essential features of older people’s independent functioning in daily life is mobility. Different aspects of mobility include for example ability to walk, climb stairs, and use public transportation. In the Health 2000 Survey, 8% of men and women aged 55–64 years and 41% of men and 52% of women aged 75–84 years reported difficulties in walking 500 meters (Sainio et al. 2006), indicating that walking limitation increases with age and is more common in women than in men. Loss of mobility seriously threatens the independence and quality of life of older adults (Ostir et al. 1998; Guralnik et al. 2000). Moreover, persons with walking limitation are less likely to remain in the community, have higher rates of mortality (Guralnik et al. 1994; Hirvensalo et al. 2000; Penninx et al. 2000; Cesari et al. 2005a) and thus need more social and health care services (Fried et al. 2001a). Consequently, prevention or postponement of walking limitation is a high priority and this requires the identification of modifiable risk factors in the older population.

Obesity is one of the potentially modifiable risk factors of walking limitation. Obesity is a rising health problem in western countries, as well as in non-industrialized countries, particularly in those undergoing economic transition (Visscher and Seidell 2001). In Finland, the prevalence of obesity (body mass index [BMI] ≥ 30 kg/m^2) has increased markedly in the adult population over the last few decades: from 12% in men and 17% in women during the late 1970s to 21% in men and 23% in women at the beginning of the 21st century (Aromaa and Koskinen 2004). While the associations between obesity and several diseases are well-established and have been studied for decades, the effect of obesity on older persons’ functional capacity has only more recently gained more systematic scientific attention. To date, only few studies have examined the negative effect of obesity on walking limitation, and relatively little is known of the possible reasons why obesity is a risk factor for poor walking performance.

Excess weight can be considered as a mechanical load which causes wear and tear on joints and reduces flexibility. The energy expenditure and oxygen consumption of an obese person engaged in a similar physical task are higher than of a normal weight person, and thus place increased demands on aerobic capacity, potentially limiting physical performance (Hulens et al. 2001; Hulens et al. 2003). In addition, due to the age-related decrease in muscle mass (Janssen et al. 2000), decreased muscle strength relative to body weight may cause difficulties in weight-bearing activities among older obese persons. Beyond these physical factors, it is likely that obesity influences walking limitation through medical conditions. Obesity is known to be an independent risk factor for several diseases (Pi-Sunyer 1993), such as type 2 diabetes, cardiovascular diseases, and knee osteoarthritis, which often restrict mobility (Stuck et al. 1999; Bootsma-van der Wiel et al. 2002). Moreover, several biological indicators related to the immune system and hormonal responses correlate with the amount of adipose tissue (Cesari et al. 2005b; Bastard et al. 2006). The association of these indicators with functional outcomes is currently under intensive investigation (Seplaki et al. 2004), thus providing new hypotheses about the pathway from obesity to walking limitation.

According to the Health 2000 Survey, the population segment with the highest prevalence of obesity consists of adults around retirement age. At the beginning of the 21st century, 28% of men aged 55–64 years and 34% of women aged 65–74 years were obese (Aromaa and Koskinen 2004). Obesity is also becoming increasingly common in young adulthood and middle-age. Earlier studies have found that in addition to current obesity, previous obesity and early onset of obesity may have adverse effects on older persons' health (Jousilahti et al. 1999; Field et al. 2001; Jeffreys et al. 2005). However, only a few studies have examined the long-term risk of obesity in earlier life on disability in later life (Guralnik and Kaplan 1989; Keil et al. 1989; Hubert et al. 1993; Vita et al. 1998; Ferraro et al. 2002; Strandberg et al. 2003; Peeters et al. 2004).

The present study was conducted to obtain knowledge about obesity as a risk factor for walking limitation in older adults. The specific objectives were to examine the role of diseases and biological indicators in the association between obesity and walking limitation, as well as to study obesity, in terms of duration of obesity, midlife obesity and physical impairments, as long-term risk factors in predicting walking limitation in later life. This study targeted Finnish men and women aged 55 years or older, and was based on the nationwide cross-sectional population-based Health 2000 Survey and the prospective Mini-Finland Follow-up Survey with a 22-year follow-up.

2 REVIEW OF THE LITERATURE

2.1 Walking as part of functional capacity

Functional capacity is a central aspect of health and well-being among older persons. In Finland, the importance of this issue has also been recognized lately on the policy level, and promotion of the functional capacity of older persons has been emphasized in the national public health program *Health 2015* (*Government Resolution on the Health 2015 public health programme* 2001). The term functional capacity refers to the ability to perform tasks and activities that people find necessary or desirable in their lives. It is a multidimensional concept and is often divided into physical, psychological, and social components. The negative aspect of functional capacity, disability, has been defined as the inability to perform or complete particular tasks or roles without difficulty or the help of another person (Verbrugge and Jette 1994). Moreover, disability can be seen as a difference or gap between an individual's ability to complete a particular task and the demands of the task (Schroll 1994).

Various conceptual models of functional capacity have been proposed. The most widely used conceptualization is *the disablement process*, which is based on the model initially proposed by Nagi (1965; 1976) and further extended and elaborated among others by Verbrugge and Jette (1994) (Figure 1). The main pathway in the disablement process is presented as sequential events starting from pathology (e.g. chronic diseases) proceeding to the generation of impairments (e.g. decreased muscle strength and aerobic capacity), and consequent functional limitations (e.g. restrictions in walking), and ending to disability (e.g. difficulties in performing the activities of daily living [ADL]). The key concept in the disablement process is *functional limitation,* the state between impairment and disability. It is defined as limitation in performance at the level of the whole organism or person (Nagi 1991), in which the individual's overall ability to perform various activities is limited. Although functional limitation is often a direct consequence of pathology and impairment, it may also arise as a direct or indirect result of prior predisposing risk factors, such as sociodemographic, lifestyle, and behavioral characteristics of an individual (Verbrugge and Jette 1994). In addition, intra-individual factors such as lifestyle and behavioral changes and psychosocial attributes, and extra-individual factors such as medical care, rehabilitation, external supports and environment may either reduce or increase functional limitation or disability.

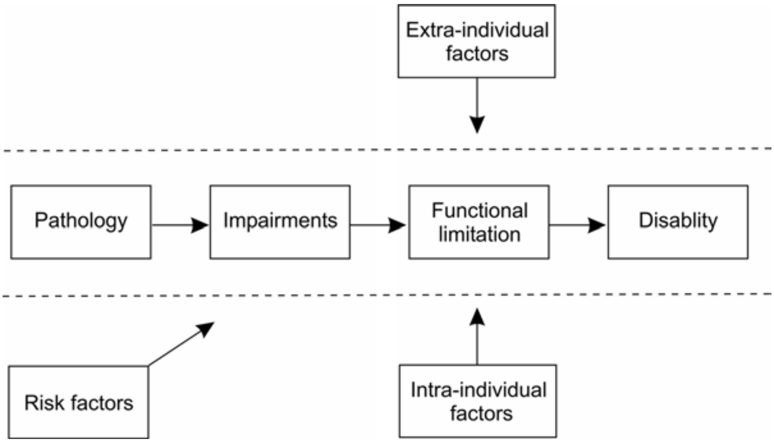

Figure 1. *A model of the disablement process (Verbrugge and Jette 1994).*

In clinical and epidemiological research on older persons, there are several advantages in focusing on the assessment of functional limitations. First, recognizing functional limitations is important because they predict more adverse outcomes such as subsequent disability (Guralnik et al. 1995; Ostir et al. 1998; Guralnik et al. 2000), hospitalization (Guralnik et al. 1994; Penninx et al. 2000), and mortality (Guralnik et al. 1994; Hirvensalo et al. 2000). Secondly, a functional limitation represents an outcome that is relatively free of the cultural and environmental influences which are likely to have a large impact on people's experiences of disability. Thus, functional limitation serves a valid outcome to indicate the effect of diseases, impairments, and other risk factors on functional capacity (Guralnik and Ferrucci 2003). Finally, persons with physical functional limitations appear to be a good target group for physical exercise interventions. They are not so disabled that they are unable to participate in interventions, and neither are they so healthy and well-functioning that small intervention effects cannot be detected (Guralnik and Ferrucci 2003; Keysor 2003).

In the present study, the focus is on one important aspect of functional limitation, namely walking limitation. Walking is a central part of daily functioning and a critical prerequisite of independent living. In gerontological research, walking performance has been found to be a very suitable indicator of functional limitation (Cesari et al. 2005a). In addition, walking as an activity is universal and little influenced by cultural differences; therefore it enables valid international or intercultural comparisons (Lan et al. 2003). Several studies during the last decade have found that walking limitation is a major risk factor for difficulty and dependency in other domains of physical functioning (Ostir et al. 1998; Guralnik et al. 2000; Shinkai et al. 2000) as well as to falling (Covinsky et al. 2001; Montero-

Odasso et al. 2005). In addition, walking limitation or impaired lower extremity performance predicts hospitalization and mortality (Guralnik et al. 1994; Hirvensalo et al. 2000; Penninx et al. 2000; Cesari et al. 2005a).

Determinants of walking limitation

Smooth and controlled walking performance is dependent on the integration of multiple physiological, cognitive, and psychological characteristics. From the physiological point of view, walking is determined and coordinated by musculoskeletal, cardio-respiratory, sensory, and neural systems (Sakari-Rantala et al. 1998). Two most important prerequisites for walking are lower extremity muscle strength and postural balance (Rantanen et al. 1999a; Tiedemann et al. 2005). These are needed to generate continuous movement to progress forward and to maintain an upright body posture during progression (Woollacott and Tang 1997). In addition to sufficient strength, walking performance requires the ability to generate force at high velocity in response to changing environmental and task demands. There is evidence that decreased muscle power (power = force x velocity) rather than decreased strength is more closely associated with impaired walking performance (Bean et al. 2003; Sayers et al. 2005). Furthermore, it has been suggested that lower extremity muscle strength and power are not linearly associated with walking speed, but instead, there are thresholds, and above a certain threshold, an increase in strength or power does not have the effect of an increasing on walking speed (Buchner et al. 1996; Ferrucci et al. 1997; Rantanen et al. 1998a).

In addition to impaired muscle strength and postural stability, decreased aerobic capacity and reduced range of motion in the lower extremity joints may restrict walking performance (Kerrigan et al. 1998; Bean et al. 2002). Also impaired vision, especially distant visual acuity and contrast sensitivity, as well as increased reaction time may cause difficulties in maintaining stability and responding to environmental changes while walking (Sakari-Rantala et al. 1998; Cromwell et al. 2002; Tiedemann et al. 2005).

Other underlying causes of poor walking performance include diseases and other medical conditions. Potentially fatal diseases that are known to cause mobility limitation are coronary heart disease through its manifestations of angina pectoris and myocardial infarction as well as through its complications, such as heart failure (Guralnik et al. 1993; Bootsma-van der Wiel et al. 2002). Also hypertension, claudication, stroke, pulmonary diseases, and type 2 diabetes are strong predictors of walking limitation through their effects on the cardiopulmonary and peripheral nervous system (Guralnik et al. 1993; Gregg et al. 2002; Volpato et al. 2003; Al Snih et al. 2005; Figaro et al. 2006; Shah et al. 2006). Of the nonfatal diseases, arthritis is the leading cause of mobility limitation. In particular painful arthritis in the lower extremities may strongly limit mobility (Ettinger et al. 1994; Ling et al. 2003).

According to the model of the disablement process presented by Verbrugge and Jette (1994), there are several other risk factors that may cause functional or walking limitation either independently or through the above mentioned diseases and physical impairments. Risk factors related to health behavior causing functional limitation include smoking, heavy alcohol use, obesity, and physical inactivity (Ebrahim et al. 2000; Wannamethee et al. 2005a; Cawthon et al. 2007). With regard to older persons' walking ability, physical activity has a major role in maintaining physical performance (Keysor 2003). Furthermore, due to an almost epidemic increase in obesity in the western countries, obesity has been acknowledged as a major risk factor for functional limitation in older people (Zamboni et al. 2005).

Measurement of walking limitation

The most obvious change in older persons' walking is a substantial decrease in speed with age (Ferrandez et al. 1990). This has been found in both cross-sectional (Bohannon 1997; Sainio et al. 2006) and longitudinal studies (Seeman et al. 1994; Sonn et al. 1995; Era and Rantanen 1997). According to the nationally representative Health 2000 Survey, 7% of men and 11% of women aged 55–64 years had a walking speed of less than 1.2 m/s, whereas in the age group 75–84 years old the corresponding proportions were 49% and 67% (Sainio et al. 2006). The decline in walking speed is mainly due to decreased stride length and longer duration of the double-support phase where both feet are on the ground (Ferrandez et al. 1990; Ostrosky et al. 1994; Frank and Patla 2003). Besides the physiological restrictions in muscle strength, joint range of motion and vision can change the normal walking pattern, as well as poor balance and fear of falling may decrease walking speed and shorten stride length (Ferrandez et al. 1990; Alexander 1996).

Walking ability in older persons can be measured in several ways, depending on the available equipments, room, time, and financial resources. Of the available physical performance measures, walking speed has been widely recognized as a good measure of mobility limitation both for healthy and impaired older persons (Guralnik et al. 1995). Because measurement of walking speed is quick, inexpensive, highly reliable, and sensitive to change it is a very practical method in the standard clinical setting as well as in large epidemiological studies (Onder et al. 2002; Ostir et al. 2002; Cesari et al. 2005a). Moreover, as mentioned earlier, walking speed has high predictive validity for subsequent disability, hospitalization, and mortality (Guralnik et al. 2000; Cesari et al. 2005a).

Currently, several test versions of measuring walking speed are used. First, the walking distance in the walking speed test varies between studies, the three most often used distances are 2.4 meters (8 feet) (Guralnik et al. 1994; Markides et al. 2001), 4 meters (Rantanen et al. 1999a; Studenski et al. 2003), and 6.0 or 6.1 meters (20 feet) (Bassey et al. 1992; Fiatarone et al. 1994; Visser et al. 2002a). In Finland a 10-meter walking course is most often used (Sakari-Rantala et al. 1995; Avlund et al. 2006). Secondly, the subject can be instructed to walk at either maximal or usual pace. The first-mentioned indicates the capacity of the neuromuscular system, thus giving an idea of the individual's potential to adapt to varying environmental and task demands (e.g. crossing a street), and the latter shows the normal performance level in everyday life. As can be seen, walking speed is usually measured using quite a short walking distance. However, long-distance walking tests provide more specific information about the aerobic capacity of older persons. The two most often used measures are the 6-minute walking test (Guyatt et al. 1985; Lord and Menz 2002) and the long-distance corridor walk (400 m) (Simonsick et al. 2001a). Although these measures provide relevant information about the overall mobility and functional capacity of older persons (Bean et al. 2002; Lord and Menz 2002), they are not as widely used as the above-mentioned walking speed tests. This is mainly due to the longer test duration.

In addition to objective walking tests, walking limitation can be assessed with self-reported measures based on questionnaires and interviews; self-reports are often used in large-scale studies. In general, individuals are asked about their ability, difficulties, or need for help in walking a certain distance. The distances that are often used in questionnaires include 400 meters (1/4 mile or 2–3 blocks) (Hoeymans et al. 1996; Rantanen et al. 1999a; Sayers et al. 2004), 500 meters (Aromaa et al. 1989; Sainio et al. 2006), and ½ mile (800 m) (Rosow and Breslau 1966; Guralnik et al. 1994; Reuben et al. 2004). These simple questions referring to a meaningful distance for older adults, as well as to long-distance walking tests, have been found to predict future disability (Guralnik et al. 1994; Reuben et al. 2004).

2.2 Obesity and body composition

Definition and measurement of obesity and body composition

Obesity is defined as a condition of abnormal or excessive fat accumulation in the adipose tissue, to the extent that health may be impaired (World Health Organization 2000). Weight gain is caused by a positive energy balance stemming from an imbalance between energy intake and energy expenditure. The three major causes of this imbalance are metabolic factors, diet, and physical activity, and each of which is influenced by genetic traits (Weinsier et al. 1998). Body mass index (BMI), waist circumference, and waist-to-hip ratio (WHR) are so far the most commonly used anthropometric measures for the classification of general and central obesity (World Health Organization 2000). BMI, which was developed by the Belgian mathematician Quetelet in the 19th century, is a simple index measuring general adiposity and it is defined as weight in kilograms divided by height squared in meters (kg/m^2). The World Health Organization (WHO) (2000) and the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults (1998) have proposed an international classification of overweight and obesity which is based on results concerning the risk of morbidity and mortality according to relative weight in different populations. According to the WHO (2000), a BMI < 18.5 kg/m^2 is defined as underweight, 18.5–24.9 kg/m^2 as normal weight, 25–29.9 kg/m^2 as overweight, and ≥ 30 kg/m^2 as obesity. Obesity can be further divided into moderate obesity (30–34.9 kg/m^2), severe obesity (35–39.9 kg/m^2), and very severe obesity (≥ 40 kg/m^2).

Abdominal obesity can be easily assessed by measuring waist circumference and WHR. Waist girth is measured at the midpoint between the lower border of the rib cage and the iliac crest, and hip girth is assessed at the widest part of the pelvis. In epidemiological studies, classification of waist circumference and WHR are often based on gender and population specific percentiles (e.g. quartiles or quintiles), but general cut-off points to define increased health risks have also been presented. Widely used cut-off points for waist circumference are 1.02 meters in men and 0.88 meters in women, and for WHR 1.0 in men and 0.85 in women (World Health Organization 2000). In Finland according to the Current Care guidelines (2002), for waist circumference the values of 1.00 meters for men and 0.90 meters for women are deemed to indicate increased health risk. To control for the effect of body height on waist circumference, waist-to-height ratio has also been proposed as a measure of abdominal fat (Han et al. 1997). However, it is not used as widely as waist circumference. When waist circumference and WHR have been compared, waist circumference has been found to have a higher correlation with the amount of visceral fat than WHR and a stronger association with poor health than WHR (Pouliot et al. 1994; Lean et al. 1995; Stewart et al. 2003). In addition, in older persons loss of muscle mass from the hip area may lead to overestimation of WHR

(Molarius and Seidell 1998). Therefore, it has been suggested that waist circumference could be used alone to indicate abdominal fat distribution.

Several other tools are available for more detailed characterization of the obesity state. Body composition and body fat mass can be measured accurately, for example with underwater weighting and dual X-ray absorptiometry (DXA). The distribution of body fat can be measured in anatomical detail by using sophisticated imaging techniques, such as magnetic resonance imaging (MRI) and computed tomography (CT) (Jebb and Elia 1993; Goodpaster 2002). However, they are relatively difficult to use, and the costs of such techniques in terms of time and money limit their usefulness in large epidemiological studies and in routine clinical practice. Nevertheless, there are some exceptions. Bioelectrical impedance analysis (BIA), for example, provides valid body composition estimates at relatively low cost and it is easy to use and is not time-consuming (Jebb and Elia 1993; Kyle et al. 2004).

Age-related changes in body composition

When assessing obesity in an older population, age-related changes in anthropometrics and body composition must be taken into account. Body height declines with aging, faster in women than in men, mainly because of the loss of mineral content from the vertebral body due to osteoporosis and to the thinning of the inter-vertebral discs, which results from changes in the fibrocartilage quality of the annulus fibrosus and hydration level of the nucleus pulposus (Sorkin et al. 1999; Sagiv et al. 2000). There is little decline in height until the age of 40. However, height starts to decrease more strongly after the age of 60 in men and 50 in women (Sorkin et al. 1999). Sorkin et al. (1999) demonstrated that cumulative height loss from age 30 to 70 years averaged about 3 centimeters for men and 5 centimeters for women, and by age 80 years was around 5 centimeters for men and 8 centimeters for women. Contrary to body height, body weight tends to increase, peaking at about age 60 years in men and later in women (Noppa et al. 1980; Rissanen et al. 1988; Droyvold et al. 2006). This can be partly explained by the progressive decline in total energy expenditure with aging and it is primarily due to decreased physical activity and in part a decrease in the basal metabolic rate (Elia et al. 2000).

In addition to an increase in fat mass, aging is also associated with a redistribution of fat in the body: visceral fat increases, while subcutaneous fat in other regions of the body decreases (Zamboni et al. 1997; Beaufrère and Morio 2000). Also the amount of fat in muscle increases (Ryan and Nicklas 1999; Goodpaster et al. 2000). After the age of 70 most persons experience a decrease in weight and the average loss is 2–3 kilograms during each successive decade (Bassey 1998; Dey et al. 1999). Later life weight loss is mainly due to loss of lean body mass rather than decline in fat mass (Suominen 1997). Muscle mass begins to decline around the age of 30 years with a more accelerated loss after the age of 60 (Lexell et al. 1988; Janssen et al.

2000). The loss is greater in men than in women in both absolute terms and relative to body weight (Gallagher et al. 2000; Hughes et al. 2001). Physical sedentariness, hormonal changes, malnutrition, loss of neuromuscular function, and chronic diseases have been found to accelerate the loss of muscle mass (Morley et al. 2001; Doherty 2003; Roubenoff 2003).

Adverse health effects related to obesity

The negative effect of obesity on health is well-known. Both cross-sectional and longitudinal studies have shown that obesity is a major risk factor for type 2 diabetes, insulin resistance, elevated blood pressure, and coronary heart disease as well as for other chronic conditions such as osteoarthritis, cancer, sleep apnea, and some respiratory conditions (Pi-Sunyer 1993; National Institutes of Health 1998; World Health Organization 2000). Especially hazardous for metabolic disorders and coronary heart disease is excess fat in the abdominal area (Silventoinen et al. 2003; Wannamethee et al. 2005b). In addition to medical outcomes, obesity among older persons decreases physical functional capacity and quality of life (Han et al. 1998; Friedmann et al. 2001; Davison et al. 2002; Larsson et al. 2002; Houston et al. 2005a). In contrast, the relationship between overweight, obesity and mortality among older people remains controversial, mainly because of many confounding factors (Zamboni et al. 2005; Al Snih et al. 2007). Most studies have reported that obesity is associated with increased mortality, but moderate overweight does not seem to increase the risk of death (Heiat et al. 2001).

2.3 The effect of obesity on walking limitation

A growing number of studies have found that excess body weight among older people is associated with poor mobility, and it also exposes to subsequent mobility limitation (LaCroix et al. 1993; Launer et al. 1994; Ebrahim et al. 2000; Bannerman et al. 2002; He and Baker 2004; Jenkins 2004; Houston et al. 2005a; Angleman et al. 2006; Mendes de Leon et al. 2006). The focus in the studies so far has been mainly on the association between BMI and mobility limitation. Few studies have been attempted on abdominal obesity measured by waist circumference, despite that there is a tendency towards an increase of abdominal fat with aging (Zamboni et al. 1997; Rössner 2001). However, according to recent cross-sectional (Ramsay et al. 2006) and prospective studies (Bannerman et al. 2002; Houston et al. 2005a; Angleman et al. 2006; Guallar-Castillón et al. 2007) a large waist circumference has been found to be related to mobility limitation; but non-significant association has also been reported (Visser et al. 1998a). Furthermore, some researchers have used BIA, DXA and CT as objective measures of body fat mass, and found an association between body fat mass and mobility limitation (Visser et al. 1998a; Visser et al. 1998b; Broadwin et al. 2001; Sternfeld et al. 2002; Visser et al. 2002a; Visser et al. 2005; Lebrun et al. 2006; Ramsay et al. 2006).

A summary of the studies that have examined the effect of obesity on mobility limitation is presented in Appendix 1. Most of these studies have been implemented for both men and women. However, only a few studies have examined the effect of obesity on mobility limitation separately in men and women. In studies where BMI was used as an explanatory variable, the association was found to be weaker in men than in women (Davison et al. 2002; Larrieu et al. 2004; Angleman et al. 2006), except in one study (LaCroix et al. 1993). There are also a few gender-stratified studies where waist circumference and body fat mass have been used as explanatory variables (Visser et al. 1998a; Broadwin et al. 2001; Angleman et al. 2006; Guallar-Castillón et al. 2007). However, comparison of the results between men and women is more difficult due to gender-specific categorization of waist circumference and body fat mass.

Due to the fact that a great majority of studies referred to in Appendix 1 are large-scale epidemiological studies, the results are often based on self-reported body weight and height and/or self-reported difficulties in mobility-related tasks. There is evidence that people tend to underestimate their body weight and overestimate their body height, thus causing underestimation of BMI (Kuskowska-Wolk et al. 1992; Engstrom et al. 2003), and consequently also underestimation of the risk of mobility limitation associated with overweight and obesity. In addition, cognitive status and depressive symptoms may have an influence on self-reported mobility limitations (Kempen et al. 1996; Hoeymans et al. 1997), thus potentially causing misclassifications (Guralnik et al. 1994). In studies related to BMI or waist circumference, only Angleman et al. (2006), Davis et al. (1998), and Mendes de Leon et al. (2006) have used objectively measured indicators of obesity and mobility. Thus, there is need for further studies on the association between obesity and mobility limitation as well as on the effect of gender on that association, using objectively measured indicators of obesity and mobility limitation.

As can be seen in Appendix 1, several longitudinal studies have been produced on the predictive role of obesity on subsequent mobility limitation. In addition to short-term follow-up studies, it is important to gain knowledge about the potential risk factors in early adulthood and midlife to later mobility limitation. However, only two long-term follow-up studies where the follow-up time is longer than 10 years and the effect of previous obesity on later life walking limitation has been published (Launer et al. 1994; Ebrahim et al. 2000). In their study Launer et al. (1994) found that the 45- to 59-year-old and 60- to 74-year-old women in the highest BMI tertile had a two-fold higher risk for developing mobility limitation over an average follow-up 14 years than women in the lowest BMI tertile. In addition, Houston et al. (2005b) found that recalled weight at age 25 was significantly associated with functional limitation in late adulthood, but no information about possible baseline functional limitation was available in their study. Furthermore, studies related to late-life ADL disabilities have shown that excess weight in middle age predicts late-life disability (Guralnik and Kaplan 1989; Keil et al. 1989; Hubert et al. 1993; Vita et al. 1998; Ferraro et al. 2002; Peeters et al. 2004). In addition to obesity in midlife, early onset of obesity and obesity duration may have adverse effects on mobility in older persons. There is evidence that the risk of type 2 diabetes (Sakurai et al. 1999; Wannamethee and Shaper 1999; Janssen et al. 2004; Jeffreys et al. 2005) and metabolic syndrome (Janssen et al. 2004) increases with obesity duration. However, no previous studies have examined the effect of obesity history on walking limitation.

2.4 Mediating factors between obesity and walking limitation

Information on the possible mechanisms leading from obesity to mobility limitation is limited. A search of the literature found only two studies in which the possible mediators between obesity and mobility limitation were investigated (Clark and Mungai 1997; Jenkins 2004). The negative effect of obesity on mobility is probably multifactorial, and consists of different pathological states, i.e. chronic diseases, physical impairments, and lifestyle factors such as physical inactivity. In Figure 2 (page 27), a hypothetical model of the effects of obesity on the pathway to walking limitation is presented. However, beyond the mediating factors presented in the model, excess body weight as such may decrease physical performance since the additional loading on the locomotor system increases energy expenditure and therefore oxygen consumption (Hulens et al. 2001; Hulens et al. 2003). Obesity may also cause strain, pain or reduced range of motion in the lower limb joints, friction of the skin or urinary incontinence, thus limiting walking or other weight-bearing activities such as stair climbing (Mommsen and Foldspang 1994; Messier et al. 2005; Wearing et al. 2006).

Presumably, medical conditions constitute one of the most important pathways from obesity to walking limitation. Obesity is known to be associated with several diseases, such as type 2 diabetes, heart diseases, hypertension, and osteoarthritis (Pi-Sunyer 1993) which in turn are known risk factors for walking limitation (Guralnik et al. 1993; Stuck et al. 1999; Bootsma-van der Wiel et al. 2002). In a study on 30- to 70-year-old African-American women, diabetes, arthritis, pain, and visual impairment partially explained the association between high BMI and mobility difficulties (Clark and Mungai 1997). Moreover, Jenkins (2004) found that diseases, symptoms and strength impairment partially explained the relationship between BMI and mobility impairment among older Americans. Unfortunately, more detailed information on the effect of individual diseases was not available in that study, as diseases formed a single group variable.

In addition to diseases, there are several biological indicators related to the immune system and hormonal responses, which may partially explain the effect of obesity on walking limitation. Recently, an extensive number of associations between biological indicators and various functional outcomes has been proposed (Seplaki et al. 2004). One of the strongest predictors of functional decline is low-grade inflammation through its catabolic effects on muscle (Ferrucci et al. 2002; Kuo et al. 2006). Cross-sectional and prospective studies have shown that increases in inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), correlate with decreases in muscle mass and strength (Visser et al. 2002b; Pedersen et al. 2003; Cesari et al. 2005b; Schaap et al. 2006), as well as mobility limitation (Ferrucci et al. 2002; Cesari et al. 2004; Penninx et al. 2004; Figaro et al. 2006; Kuo et al. 2006). Moreover, low-grade inflammation has been found to be related to obesity (Festa et al. 2001; Forouhi et al. 2001; Cesari et al. 2005b; Thorand et al. 2006). Research suggests that cytokines, for example IL-6 and tumor necrosis factor-α (TNF-α), are released into circulation from the adipose tissue (Mohamed-Ali et al. 1997), and IL-6 further stimulates the production of acute-phase proteins, such as CRP in the liver (Baumann and Gauldie 1994). Thus, these factors might partially explain the association between excess body fat and inflammatory markers (Festa et al. 2001; Forouhi et al. 2001).

An important determinant of walking performance, muscle strength, may also have an independent effect on an obese person's physical performance beyond the effects of inflammation. In absolute terms, obese persons may have higher muscle strength than normal weight individuals. However, when adjusted for body size, muscle strength is often lower in obese than normal weight subjects (Wearing et al. 2006). Thus, decreased muscle strength relative to body weight often exposes obese persons to limitations in walking and other weight-bearing activities. In gerontological research, the presence of excess fat in combination with decreased muscle mass, i.e. sarcopenia, is called sarcopenic obesity (Baumgartner 2000; Roubenoff 2000). There is some evidence that sarcopenic obesity may be associated with impaired walking and precede the onset of disability (Baumgartner 2000; Baumgartner et al. 2004). However, non-significant associations have also been reported (Davison et al. 2002; Zoico et al. 2004). Currently, there is evidence that muscle strength may be more important than muscle mass as a determinant of functional limitation and health in older age (Visser et al. 2000; Visser et al. 2005; Newman et al. 2006), thus the hypothesis about the effect of concurrent obesity and low muscle strength on walking limitation needs to be investigated further.

Health behavioral factors, especially physical inactivity may in part mediate the effect of obesity on walking limitation. Obesity and physical inactivity are known to be closely connected, as are physical activity and physical functional capacity

(Brach et al. 2003; Bernstein et al. 2004; Brach et al. 2004a). Obese persons tend to be physically more sedentary than normal weight persons. Furthermore, physical inactivity correlates with low muscle strength, decreased aerobic capacity and impaired balance, thus consequently impairing walking and other mobility-related activities.

2.5 Coexisting conditions and walking limitation

With aging, the prevalence of diseases increases markedly and may lead to the coexistence of multiple chronic conditions, commonly referred to as comorbidity. Fried et al. (2004) have defined comorbidity as the concurrent presence of two or more medically diagnosed diseases in the same individual. Similarly, older people may simultaneously have two or more physical impairments. This state is called coimpairment. Nowadays, the effects of a single disease or a single physical impairment on mobility are relatively well known, but there is a paucity of studies on the effect of comorbidity and coimpairment on functional limitation. Rantanen and coworkers (1999a; 2001) found that co-occurrence of low muscle strength and impaired balance in older women is associated with severe walking disability. In addition, they suggested that the negative effect of impairment in one physiological system may be compensated by good capacity in another physiological domain. Consequently, people with poor balance may manage to avoid walking difficulties if they have enough strength in the lower extremities. Furthermore, Cesari et al. (2006) reported that among older people aged 80 years or older, comorbidity, defined here as three or more coexisting conditions (diagnosed diseases or obesity), was associated with lower walking speed and poorer physical functioning than among those without comorbidity. Other researchers have similarly found that comorbidity or coimpairment increases the risk of disability and mortality more than do individual conditions (Verbrugge et al. 1989; Ettinger et al. 1994; Fried et al. 1999; Rantanen et al. 2000).

However, the effect of obesity and coexisting conditions on adverse health outcome has been investigated in only two studies. Rantanen et al. (2000) reported that the combination of overweight and low muscle strength caused the highest risk of death during a 30-year follow-up among initially healthy men compared with other BMI and muscle strength combinations. Similarly, Ettinger et al. (1994) found that obese people with knee osteoarthritis had increased risk of subsequent mobility limitation 10 years later. Further studies on obesity and coexisting conditions and their effect on walking limitation are needed to recognize more potential high risk groups among obese persons.

The hypothetical model presented in Figure 2 illustrates the potential pathways from obesity to walking limitation discussed in the previous chapters. The model is based on the theoretical model of *the disablement process* presented by Verbrugge and Jette (1994) and it enables to locate the mediating and confounding factors between obesity and walking limitation in the right order relative to each other in the disablement process. Furthermore, the main concepts and the focus of this study are also shown in Figure 2. Besides the mediating factors, the association between obesity and walking limitation will be studied by different obesity subgroups, such as concurrent obesity and chronic diseases and obesity and low muscle strength.

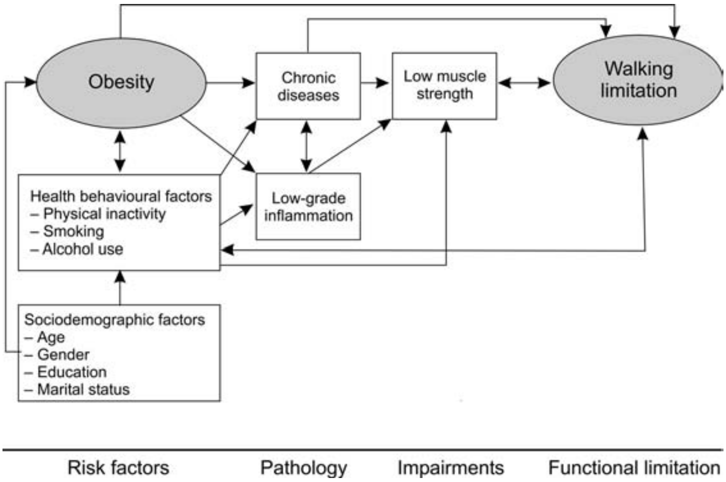

Figure 2. ***A hypothetical model showing the potential pathways from obesity to walking limitation.***

3 AIMS OF THE STUDY

This study was conducted to explore obesity as a risk factor for walking limitation, and to examine the role of chronic diseases and biological indicators in that association among Finnish men and women aged 55 years or older. In addition, obesity and physical impairments were studied as long-term risk factors in predicting walking limitation in later life.

The specific objectives of this study were:

1. To describe the association between different obesity indicators and walking limitation among men and women (Studies I and II).
2. To study whether chronic diseases and biological indicators mediate the association between obesity and walking limitation (Studies I and II).
3. To investigate obesity duration, midlife obesity and physical impairments as long-term risk factors on walking limitation in later life (Studies III and IV).
4. To study the effect of comorbidity and coimpairment on walking limitation (Studies I, II, and IV).

4 MATERIALS AND METHODS

4.1 Study designs and participants

The Health 2000 Survey

The Health 2000 Survey is a comprehensive nationwide health interview and examination survey which was implemented in Finland in 2000–2001 (Aromaa and Koskinen 2004). The two-stage stratified cluster sample comprised individuals aged 30 years and older living in mainland Finland either in the community or in institutions. The frame was regionally stratified according to the five university hospital districts, each containing approximately one million inhabitants. From each university hospital region, 16 health care districts were sampled as clusters. The 15 largest cities were all included in the sample with a probability of one, and the remaining 65 health care districts were selected by applying the systematic probability proportional to size method. Finally, from these 80 clusters (including 160 municipalities), a sample of 8 028 persons was selected by systematic sampling (Figure 3). In order to obtain a sufficient number of older people, persons aged 80 years or older were over-sampled (2:1) in relation to their proportion in the population. The study population for the present study was limited to persons aged 55 years or older (range 55–99 years), and consisted of 3 439 persons, of whom 3 392 persons, 1 337 men and 2 055 women, were alive on the day of the first phase of the survey.

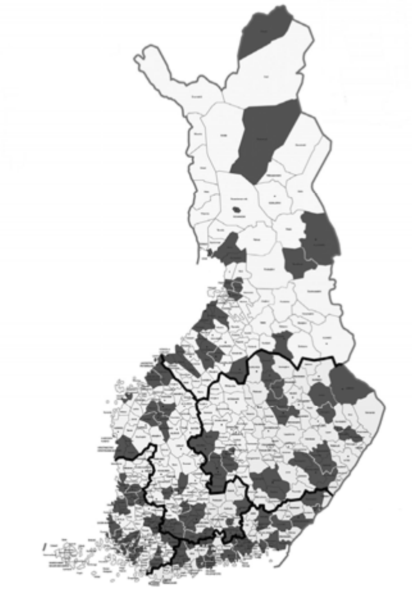

Figure 3. ***Study areas of the Health 2000 Survey. The boundaries of the university hospital districts are marked in bold line and the participating municipalities are shown in color on the map.***

A structured health interview with a mean duration of 95 minutes was completed at the participant's home, eliciting information about the person's health, illnesses, and functional ability as well as sociodemographic and health behavioral factors. If the person did not participate in the main interview, a supplementary interview was conducted later or eventually a questionnaire was sent. The overall participation rate in the health interview was 94% (n = 3 186). A few weeks later the participant attended a comprehensive health examination in a health centre. This examination consisted of several components such as measurement of anthropometry, functional capacity, and laboratory tests (n = 2 572, 76% of the sample). In addition, a structured clinical examination by a physician was completed. An abbreviated health examination was conducted at home or in an institution for those who did not participate in the study center examination (n = 306, 9% of the sample). After the examinations, a final interview was conducted and a nurse checked that the person had attended every planned measurement and that questionnaires had been properly filled in. In addition, during the health interview, the participant was given a questionnaire, which was to be returned on arrival at the health examination. This questionnaire included information for example about weight history and alcohol use, and was returned by 2 845 persons (89%). A detailed description of the study design, data collection methods, and health and functional status of the study population has been reported elsewhere (Aromaa and Koskinen 2004).

The Mini-Finland Follow-up Survey

The Mini-Finland Follow-up Survey is based on the population-based Mini-Finland Health Examination Survey implemented in 1978–1980. The baseline study population was a stratified two-stage cluster sample drawn from the national population register to represent Finnish adults aged 30 years or older (Aromaa et al. 1989). In the first stage, 40 representative areas were selected and within these areas a sample of 8 000 individuals (3 637 men and 4 363 women) were selected by systematic sampling. A total of 7 217 subjects (90% of the sample) participated. The survivors (n = 1 278) who were living in the seven selected large municipalities out of the original 40 in 2000–2001 were invited to take part in the follow-up study, which was executed as part of the Health 2000 Survey. The present study was limited to persons who reported no walking limitation (were able to walk 500 meters) and were not pregnant at the baseline, and who were 55 years or older at follow-up (n = 954). Only 11.9% (n = 114) of the eligible sample were not able or unwilling to participate in the follow-up.

The health examinations of the Mini-Finland Health Examination Survey were performed in two phases (Aromaa et al. 1989; Mäkelä et al. 1991). In a screening phase, a specific structured interview for symptoms was executed, and several examinations, including blood pressure measurements and blood sampling, were performed. In addition, a standardized joint function test for musculoskeletal impairment and a questionnaire on mental symptoms were administrated. Participants with a history of a disease, symptoms or findings suggestive of a musculoskeletal, cardiovascular, respiratory, or mental disorder were invited to participate in the main examination. This consisted of supplementary interviews, measurements and a standardized examination by a physician. Details of the design and implementation of the Mini-Finland Health Examination Survey have been reported elsewhere (Aromaa et al. 1989).

All the participants in the Health 2000 Survey as well as the Mini-Finland Follow-up Survey signed a written informed consent and the studies were approved by the Ethical Committee for epidemiology and public health in the hospital district of Helsinki and Uusimaa in Finland. The data and the inclusion criteria used in the original publications are shown in Table 1.

Table 1. *Study designs, populations and inclusion criteria in original studies*

Study	Survey	Design	Age (years)	Participants	Inclusion criteria
I	The Health 2000 Survey (n = 3 392)	Cross-sectional	55–99 (mean 67.5)	n = 2 961 (87%), 1 193 men, 1 768 women Excluded (6%) Non-participants (7%)	- Information on BMI and either measured walking speed or self-reported walking ability. - BMI ≥ 18.5 kg/m^2 and no unintentional weight loss ≥ 10kg during previous 12 months.
II	The Health 2000 Survey (n = 3 392)	Cross-sectional	55–97 (mean 66.1)	n = 2 099 (62%) 932 men, 1 250 women Excluded (31%) Non-participants (7%)	- Information on BMI, WC, body fat percentage, CRP, handgrip strength, and either measured walking speed or self-reported walking ability. - No unintentional weight loss ≥ 5 kg during previous 12 months.
III	The Health 2000 Survey (n = 3 392)	Retrospective from age of 20 years	55–99 (mean 65.8)	n = 2 034 (60%) 878 men, 1 166 women Excluded (33%) Non-participants (7%)	- Information on complete weight history and either measured walking speed or self-reported walking ability. - BMI ≥ 18.5 kg/m^2 and no unintentional weight loss ≥ 5 kg during previous 12 months.
IV	The Mini-Finland Follow-up Survey (n = 1 278)	Prospective 22 years	32–72 at baseline (mean 45.8)	n = 840 (66%) 362 men, 478 women Excluded (23%) Non-participants (12%)	- No walking difficulties and not pregnant at baseline. - 55 years or older, and either measured walking speed or self-reported walking ability at follow-up.

Notes: Percentages in parentheses indicate the proportion of individuals in each category of the total study sample. Excluded persons did not meet the inclusion criteria and non-participants did not participate either the health interview or health examination.
BMI = body mass index; WC = waist circumference; CRP = C-reactive protein.

4.2 Study variables and definitions

A summary of the variables used in the analyses in the original studies is presented in Table 2. The variables and their measurement are described in more detail in the original studies (I–IV).

Table 2. ***The variables used in the analyses in the original studies***

Variable	Study	Reference for method	Reliability
Outcome variables			
Maximal walking speed on 6.1 m (H)	I–IV	(Fiatarone et al. 1994; Sainio et al. 2005)	ICC = 0.77, n = 153 (Sainio et al. 2006)
Self-reported difficulty in walking 500 m (I)	I–IV	(McWhinnie 1981; Aromaa et al. 1989)	
Walking limitation	I–IV	See description on the page 35	
Explanatory variables			
BMI (body weight and height) (H, Q)	I–III	Weigth: Biospace, Inbody 3.0 or portable spring scale; Height: Person-Check, Medizintechnik, KaWe (Germany) or wall measure	
BMI (body weight and height)	IV	Weigth: spring scale Height: wall measure	
Waist circumference (H)	II	(Reunanen 2005)	ICC = 0.95, n = 92 (Reunanen 2005)
Body composition (body fat percentage)	II	Biospace, Inbody 3.0 (Seoul, South-Korea) (Heliövaara 2005)	
Body height at age 20 years (Q)	III	(Aromaa and Koskinen 2004)	
Body weight at age 20, 30, 40 and 50 years (Q)	III	(Aromaa and Koskinen 2004)	
Handgrip strength	IV	Bruel-Kjaer Type 1526 (Denmark) (Mälkiä 1983)	Repeatability over 3 months, r = 0.91–0.93, n = 449 (Mälkiä 1983)
Squatting	IV	(Sievers et al. 1985)	Repeatability over 3 months, K =0.66, n = 793 (Heliövaara et al. 1993)
Self-reported difficulty in running 500 m (Q)	IV	(Mälkiä 1983)	Repeatability over 3 months, K = 0.59, n = 392 (Mälkiä 1983)

Continued overleaf

Table 2 continued

Variable	Study	Reference for method	Reliability
Mediating variables			
C-reactive protein	II	Ultra-sensitive immunoturbidometric test (Orion Diagnostica, Espoo, Finland) and the Optima analyzer (Thermo Electron Corporation, Vantaa, Finland)	CV = 4.5%
Handgrip strength (H)	II	Good Strength, IGS01 (Metitur Oy, Jyväskylä, Finland). A modification of the method presented by Viitasalo et al. 1985 (Sainio et al. 2005)	ICC = 0.95, n = 265 (Sainio et al. 2005)
Medical diseases, clinical examination by physician	I–III	Structured and uniform diagnostic criteria based on current clinical practice (Aromaa and Koskinen 2004)	
Diseases, self-reported (I)	I, III	(Aromaa and Koskinen 2004)	
Diseases, clinical examination by physician	IV	Good treatment practice as a reference (Aromaa et al. 1985; Sievers et al. 1985)	Sensitivity for knee osteoarthritis 0.94, n = 740 (Heliövaara et al. 1993)
Confounding variables			
Age	I–IV		
Gender	I–IV		
Education (I)	I–IV	(Aromaa et al. 1989; Martelin et al. 2004)	
Marital status (I)	I		
Smoking (I)	I–IV	(Aromaa et al. 1989; Uutela 2004)	
Alcohol use (Q)	I–IV	(Aromaa et al. 1989; Uutela 2004)	
Physical activity (Q)	IV	(Mälkiä 1983)	
Medication	II	(Aromaa and Koskinen 2004)	

Notes: H = Measurement performed also in home health examination in the Health 2000 Survey; I = Based on interview in the Health 2000 Survey; Q = Based on questionnaire in the Health 2000 Survey. ICC = intra class correlation; r = correlation coefficient; K = kappa coefficient; CV = coefficient of variation.

Walking limitation (outcome measure)

The main outcome variable in this study was walking limitation defined according to walking speed and self-reported walking difficulty. Maximal walking speed was measured over a distance of 6.1 meters starting from a standstill (Fiatarone et al. 1994). Walking aids were allowed if the person normally used them when walking. In the home health examination, a shorter distance was allowed in the walking test if it was not possible to implement the 6.1 meters course. Participants were considered to have walking limitation if their walking speed was less than 1.2 m/s or if they were unable to finish the test. For those who did not participate in the walking test, self-reported difficulty (major or minor) or inability to walk 500 meters was used to indicate walking limitation. Self-reported walking difficulty was assessed in the interview by the question: "Are you able to walk about half a kilometer without resting?" The four response options were: without difficulty, with minor difficulty, with major difficulty and not at all. The number of persons who did not participate in the walking test was 235 in Study I, 24 in Study II, 32 in Study III, and 98 in Study IV.

In order to confirm the association between walking speed and self-reported difficulty in walking 500 meters, Receiver operator characteristics (ROC) analysis was implemented with the sample used in Study I. The accuracy of the walking speed test in classifying persons as having or not having difficulties in walking 500 meters was determined using logistic regression models and reported as the area under the ROC curve (AUC). On the basis of the sensitivity and specificity values of various walking speed cut-off points shown in Figure 4, the ROC curve was generated. The area under the ROC curve was 0.892 indicating that the walking speed test predicted self-reported walking difficulties with a high degree of accuracy. The greatest diagnostic accuracy (fewest false positives and false negatives) was found at the 1.2 m/s cut-off point (sensitivity 79%, specificity 84%), which was therefore used as the cut-off point for walking limitation in this study.

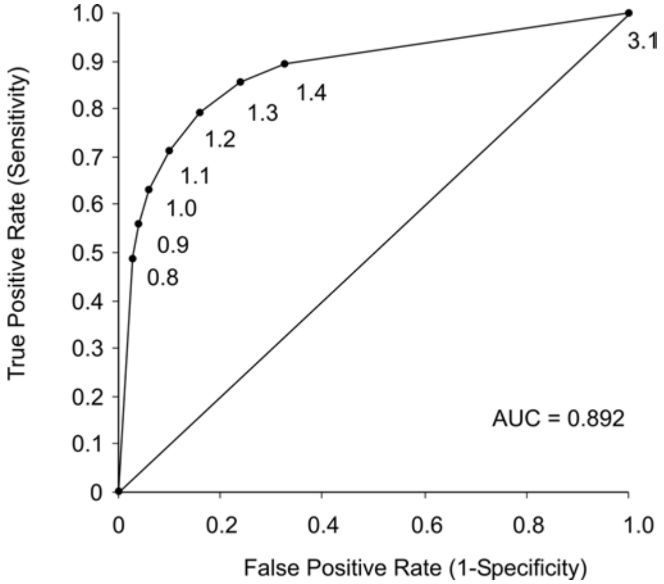

Figure 4. ***Receiver operator characteristics (ROC) curve generated from the sensitivity and specificity of different cut-off points for walking speed (m/s). Area under the ROC curve (AUC) is indicated in the figure.***

Obesity indicators (explanatory variables)

Body mass index was calculated by dividing body weight (kg) by the height squared (m^2). The measurement was performed with the participant wearing light indoor clothing without shoes, weight was measured to the nearest 100 grams and standing height to the nearest 0.5 centimeters. For those who did not attend health examinations self-reported body weight and height were used. The need to use self-reported information on weight and height was infrequent: only 7% (n = 207) in study I and less than 1% (n = 18) in study III. In the Health 2000 Survey, BMI was considered a categorical variable since the risk of disability associated with BMI is not assumed to be linear (Galanos et al. 1994; Mendes de Leon et al. 2006). BMI was classified into five categories: underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obesity (BMI 30–34.9 kg/m^2), and severe obesity (BMI $\geq$ 35 kg/m^2) (World Health Organization 2000). Normal weight was chosen, a priori, as the reference category for the multivariate analyses.

Waist Circumference was measured on the naked skin at the end of a light expiration with the person standing, and the result was rounded to the nearest 0.5 centimeter.

Because no standard international criteria for waist circumference classification are available, in study II waist circumference was divided into gender-specific quartiles. The cut-off points for the gender-specific quartiles were 0.925, 0.995, and 1.07 meters (range 0.72–1.49 m) in men and 0.835, 0.92 and 1.00 meters (range 0.59–1.62 m) in women. *Body fat percentage* was measured with eight-polar bioelectrical impedance analysis (BIA) (InBody 3.0, Biospace, Seoul, South-Korea). The gender-specific cut-off points for the body fat percentage quartiles were 20.8, 25.0, and 29.1 (range 9.3–44.6) in men, and 31.4, 35.6 and 40.0 (range 13.9–56.6) in women. The lowest quartiles for waist circumference and body fat percentage were considered the reference categories in the analyses.

Obesity history classification was based on information about current BMI as well as BMI at the ages of 20, 30, 40, and 50 years. Past BMIs were calculated according to recalled height at the age of 20 and weight at the ages of 20, 30, 40, and 50 years. On the basis of previous studies, it was assumed that body height had not changed substantially between the age of 20 and 50 years (Stafford et al. 1998; Sorkin et al. 1999). According to BMI at the given ages, participants were dichotomized into non-obese (< 30 kg/m^2) and obese (≥ 30 kg/m^2). Furthermore, they were categorized according to duration of obesity: 1) never obese, 2) previously obese, but currently non-obese, 3) currently obese, but non-obese at the ages of 20–50 years, 4) obese since age 50 years, 5) obese since age 40 years, 6) obese since age 30 years. Those who had been obese since age 20 years (n = 3) were merged with the last category. Persons who were currently obese but non-obese at age 50 years yet obese at age 30 or 40, years were excluded from the analyses (n = 11).

Physical impairments (explanatory variables)

In study IV, a set of physical impairments was determined to indicate early predictors of walking limitation in later life. Handgrip strength, as an indicator of overall muscle strength (Rantanen et al. 1994), was measured in kiloponds (kp) using a hand-held dynamometer (Bruel-Kjaer Type 1526, Denmark) (Mälkiä 1983). One kilopond corresponds to a weight of one kilogram. Measurement was done in seated position with the elbow flexed at an angle of 110°–140° and the width of the handle was adjusted for the subject's handsize. The best result of the stronger hand was used in the analyses. The cut-off points for the gender-specific handgrip strength tertiles were 50 and 58 kiloponds in men (range 15–87 kp) and 27 and 33 kiloponds in women (range 9–52 kp). The lowest tertile is referred to as impaired strength. General fitness was examined by the question: "Can you run a longer distance (about 500 meters)?" The four response categories were: without difficulty, with minor difficulty, with major difficulty, or not at all. The last two categories were combined to represent impaired fitness in middle-aged individuals. Lower limb performance was assessed by a squatting test (Sievers et al. 1985). Participants were asked to squat and stand up once. They were allowed gently to take support from a table to keep their balance. A trained nurse observed and evaluated the performance: normal (thighs at least on the horizontal level), impaired (thighs above horizontal level, but an angle of lean more than 45°) or unable (thigh angle of lean less than 45°). For this study, the categories impaired and unable were merged to indicate impaired squatting in middle-aged persons.

Mediating and confounding factors

In the Health 2000 Survey, handgrip strength was measured in Newtons (N) in the dominating hand using a hand-held dynamometer (Good Strength, IGS01, Metitur Oy, Jyväskylä, Finland) (Sainio et al. 2005). Measurement was performed with the person in the seated position, elbow flexed at an angle of 110°, wrist in the neutral position, and the interphalangeal joint of the index finger an angle of 90°. The cut-off points for the gender-specific quartiles were 334, 407, and 476 Newton (range 73–760 N) in men and 168, 221 and 269 Newton (range 13–525 N) in women (Study II). Blood samples for sensitive C-reactive protein (CRP) determination were drawn during the clinical examination after fasting for four hours. The cut-off points for the CRP quartiles were 0.41, 1.09, and 2.72 mg/l (range 0.10–191 mg/l) (Study II).

In the Health 2000 Survey (Studies I–III), a specially trained physician ascertained the medical conditions of those persons who attended the study center health examination by using structured, uniform diagnostic criteria based on current clinical practice. For those who did not attend the health examination, a self-report of diseases diagnosed by a physician was used, based on answers to the question: "Has a doctor ever told you that you have…?", followed for a list of 42 separate medical conditions. In addition, anti-inflammatory drugs and estrogen replacement therapy during the preceding 7 days was determined by checking the names of drugs from the package or prescription (Pradhan et al. 2002; Prasad 2006) (Study II). At the baseline of the Mini-Finland Follow-up Survey (Study IV), specially trained physicians ascertained the presence of chronic conditions in a clinical examination by combining the results of measurements and biochemical analyses with information gathered from interviews and questionnaires, using current good treatment practice as a reference (Aromaa et al. 1985; Sievers et al. 1985).

The sociodemographic variables used in the present series of studies were gender, age, education, and marital status. Smoking and alcohol use were elicited in interviews and questionnaires as indicators of health behavior. In addition in study IV, level of habitual leisure time physical activity was used. Accordingly, participants were classified as regular physical exercise (e.g. running, biking, gymnastics), occasional physical exercise or physically active hobbies (e.g. gardening, hunting, outdoor recreations), and little physical exercise (e.g. reading, watching television).

The above-mentioned covariates have been shown to be related to obesity and walking limitation (Stuck et al. 1999; Bootsma-van der Wiel et al. 2002) and were thus considered to be potential mediators or confounders in the association between obesity and walking limitation. Associations between these variables and walking limitation or obesity indicators were checked before the analyses. In addition to mediating and confounding factors, some variables may moderate the way in which obesity and walking limitation are related. In this study, age, gender, chronic diseases, CRP, and handgrip strength were considered to be potential effect-modifiers of the association between obesity and walking limitation and the interaction effects of these variables and obesity on walking limitation were tested.

4.3 Statistical methods

This is an observational study on the association between obesity and walking limitation as well as the factors that mediate the association, and it is based on three different study designs. Studies I and II are cross-sectional studies on a representative sample of the Finnish population aged 55 years or older. Cross-sectional studies are valuable in studying the associations between variables, but they do not contain information about the timing of explanatory and outcome variables. Thus, to learn about causal relationships between variables requires a longitudinal design. Study IV is a prospective study with a 22-year follow-up. Long-term prospective studies are especially important in gerontological research as they enable the age-related changes in various health indicators to be explored. With prospective studies it is also possible to recognize factors that increase or decrease the risk of later life adverse health outcomes such as functional limitation, disability, diseases, and death. Study III is a retrospective study which includes information about the participants' weights since the age of 20 years. Although retrospective studies based on recalled information provide less reliable information about the explanatory variables than prospective studies, they nevertheless have the power to establish the causal order of predictors and outcomes.

In this study, age- and gender-adjusted prevalence or incidence of walking limitation in different obesity categories was calculated using logistic regression models. The linearity of the association between the obesity indicators and walking limitation was tested either with the Cochran-Armitage Trend test (Study I) or with the generalized linear model (GLM) procedure of the SAS statistical package (Studies II–IV). In study III, differences in the prevalence of walking limitation between gender and the obesity history categories were calculated with Cochran-Mantel-Haenszel tests. The interaction effects of gender*obesity indicators and age*obesity indicators on walking limitation were also tested (surveylogistic). Only in study I a statistically significant interaction was found between gender and BMI ($p = 0.03$), and therefore in that study the analyses were conducted separately for men and women. The normality of the distribution of continuous variables like BMI, waist circumference, body fat percentage, walking speed, handgrip strength, and CRP was tested with the Kolmogorov-Smirnov test. Due to the skewed distribution of CRP values, the analyses concerning continuous CRP were performed using its log values.

With respect to walking limitation as a dichotomous dependent variable, logistic regression models were used to analyze its association with the different obesity indicators. The results were presented as Odds Ratios (OR) with 95% confidence intervals (CI). In each study, a hierarchical set of logistic regression models was constructed, and the age- and gender-adjusted model served as the base model (in study I the base model was age-adjusted). The chosen covariates were then adjusted sequentially in logical groups, including sociodemographic factors (education and marital status), health behavioral factors (smoking, alcohol use and physical activity), medical conditions and biological indicators (CRP and handgrip strength). The models in which handgrip strength was included were also adjusted for body height, since handgrip strength is known to correlate strongly with body size (Rantanen et al. 1998b).

The reference categories for the obesity indicators were normal weight for BMI, never obese for obesity history, and the lowest quartile for waist circumference and body fat percentage. In study IV, in addition to the obesity indicators the independent variables included handgrip strength, running, and squatting. The reference categories for the 500 meters running and squatting test were “no difficulties” and “normal”. The association of BMI, as well as handgrip strength, with walking limitation was found to be linear (tested with SAS-GLM procedure). BMI and handgrip strength were therefore used as continuous variables in the logistic regression models. In studies I and II, the individual effect of each covariate on the association between the obesity indicators (BMI, waist circumference, body fat percentage) and walking limitation was examined by adding the covariates one at a time into the age- and gender-adjusted model. The percentage reduction in ORs was then calculated as in previous studies (Lynch et al. 1996; Stronks et al. 1996; Laaksonen et al. 2005):

$$\frac{\text{OR (base model)} - \text{OR (base model + covariate)}}{\text{OR(base model)} - 1} \times 100$$

Calculations were performed only for those categories of obesity indicators that were statistically significantly associated with walking limitation in the age- and gender-adjusted model.

The associations between the potential covariates and walking limitation as well as potential covariates and obesity indicators were examined separately in each study. All the variables that were associated with walking limitation ($p < 0.05$) and linearly with obesity indicators ($p < 0.10$) were included in the logistic regression models as covariates. The association of covariates with walking limitation was tested with the χ^2-test or the Fisher exact test. For the continuous obesity indicators (BMI, waist circumference and body fat percentage) logistic regression models (Wald test) and for the categorical obesity indicator (obesity history) the SAS-GLM procedure was used to compare levels of covariates across levels of obesity indicators.

The effect of coimpairment and comorbidity on walking limitation was studied with logistic regression models by categorizing the subjects into six (study IV) and nine (study II) groups according to BMI and diseases, BMI and physical impairments (study IV) and body fat percentage and CRP and handgrip strength (study II), respectively. The interaction effects of BMI*diseases, BMI*physical impairments, fat percentage*CRP and fat percentage*handgrip strength on walking limitation were studied with the SAS-GLM procedure.

Statistical analyses were completed using SAS software version 9.1 (SAS Institute Inc., Cary, NC). For the analyses, the data were weighted to reduce the bias due to non-response and to correct for the over-sampling in the age group of 80 years and older. The complex sampling design was taken into account by using SUDAAN procedures version 9.0 (SUDAAN Language Manual, Research Triangle, NC). The numbers of subjects slightly differ for each analysis, as cases with missing values for specific covariates were excluded from the corresponding analyses.

5 RESULTS

5.1 The characteristics of the study populations

The characteristics of the participants in the Health 2000 Survey as well as in the Mini-Finland Follow-up Survey are summarized in Table 3. In the Health 2000 Survey, 23% of the participants were 55–59 years old, 37% were 60–69 years old, 28% were 70–79 years old, and 12% were 80 years or older. Age ranged from 55 to 99 year. The majority of the participants were women (57% vs. 43%). Women were older and had higher BMI and lower hand grip strength than men ($p < 0.0001$). Chronic diseases were relatively common among the participants. Hypertension (men 32% vs. women 38%, $p = 0.001$), coronary heart disease (men 21% vs. women 16%, $p < 0.0001$), and knee osteoarthritis (men 11% vs. women 18%, $p < 0.0001$) were the most prevalent conditions. Furthermore, women were more often physically sedentary, smoked less and used alcohol less than men ($p < 0.0001$). At the baseline of the Mini-Finland Follow-up Survey, 29% of the persons were younger than 40 years, 40% were 40–49 years old, 24% were 50–59 years old, and 8% were 60 years or older. Age ranged from 32 to 72 years. Mean BMI was 25.1 kg/m^2 in men and 24.4 kg/m^2 in women ($p = 0.001$). The prevalence of chronic diseases was relatively low. Men had pulmonary disease more often than women (12% vs. 7%, $p = 0.013$) and women had knee osteoarthritis more often than men (6% vs. 2%, $p = 0.005$). Women were physically more inactive than men ($p = 0.03$), but men smoked and used alcohol more than women ($p < 0.0001$).

Table 3. ***Characteristics of the participants in the Health 2000 Survey and the Mini-Finland Follow-up Survey***

Characteristic	**Health 2000 Survey** n = 2 961 Mean (SD)	**Mini-Finland Follow-up Survey*** n = 840 Mean (SD)
Age, years	67.5 (8.8)	45.8 (8.7)
Body Mass Index, kg/m^2	27.8 (4.4)	25.0 (3.5)
Handgrip strength†	306.6 (122.7)	39.8 (14.9)
	%	%
Women	57.2	56.9
Walking limitation	32.8	0
Coronary heart disease	18.1	3.3
Hypertension	35.4	8.6
Pulmonary disease	11.0	8.8
Type 2 diabetes	9.4	1.3
Knee osteoarthritis	15.1	4.2
Hip osteoarthritis	10.0	0.8
Physical inactivity	29.2	20.8
Smoking behavior		
Never smoker	59.6	54.1
Former smoker	25.4	24.1
Current smoker	15.0	21.9
Alcohol use		
Not at all	48.1	27.9
Moderate use	47.1	62.0
Heavy use	4.8	10.1
Education		
Higher (≥ 13 years)	19.6	17.3
Intermediate (10–12 years)	47.5	36.9
Basic (< 10 years)	32.9	45.8

Notes: *Baseline characteristics. †Handgrip strength was measured in the Health 2000 Survey in Newtons and in the Mini-Finland Follow-up Survey in kiloponds. In the table means and standard deviations (SDs) for the continuous variables, and percentages for the categorical variables are presented.

5.2 Prevalence of walking limitation by obesity indicators (I–III)

In the Health 2000 Survey, the overall prevalence of walking limitation among persons aged 55 years or over was 32%. When adjusted for age, walking limitation was more common among women (36%) than men (27%) ($p < 0.0001$). When adjusted for gender walking limitation increased linearly with increasing age from 12% among the 55- to 59-year-olds, to 20% among the 60- to 69-year-olds, 46% among the 70- to 79-year-olds and to 81% among persons who were 80 years or older (p for linear trend < 0.0001). Table 4 shows the age- and gender-adjusted prevalence of walking limitation according to the different obesity indicators. Within each obesity indicator a gender difference was observed, women having a significantly higher prevalence of walking limitation than men at the same level of obesity ($p < 0.0001$). The only statistically significant interaction between gender and obesity indicators on walking limitation was observed for BMI ($p = 0.03$).

In women, the prevalence of walking limitation increased linearly with increasing BMI from the normal weight category (BMI 18.5–24.9 kg/m^2) to the severely obese category (BMI $\geq$ 35 kg/m^2). In men the trend was also significant, but the prevalence increased steeply among those who were severely obese. As in the case of BMI, waist circumference, body fat percentage, and obesity history were linearly associated with walking limitation (p for linear trend < 0.0001). When all the potential covariates were taken into account, individuals with high BMI ($\geq$ 35 kg/m^2 in men and $\geq$ 30 kg/m^2 in women), large waist circumference (> 0.995 m in men, > 0.92 m in women), and a high percentage of body fat (> 25% in men, > 36% in women), had statistically significantly increased risk of walking limitation.

The correlations between BMI, waist circumference, and body fat percentage were moderate to high. BMI show a high correlation with waist circumference ($r = 0.90$ in men and $r = 0.85$ in women) and moderate with body fat percentage ($r = 0.75$ in men and $r = 0.86$ in women). In addition, waist circumference and body fat percentage show a moderate correlation ($r = 0.73$ in men and $r = 0.78$ in women). Among persons classified as obese according to BMI, 95% were in the two highest quartiles for waist circumference (> 0.995 m in men, > 0.92 m in women) and 93% were in the two highest quartiles for body fat percentage (> 25% in men, > 36% in women). 78% of persons who were in the two highest quartiles for waist circumference were also in the two highest quartiles for body fat percentage.

Table 4. ***Prevalence of walking limitation by obesity indicators and gender in the Health 2000 Survey***

		Men [1]			Women [1]		Total [1,2]	
Body mass index (kg/m^2)		n = 1 158	%		n = 1 737	%	n = 2 895	%
< 18.5		5	26.4		29	37.5	34	32.7
18.5–24.9		336	22.1		512	31.3	848	27.5
25–29.9		540	21.7		686	34.8	1226	29.3
30–34.9		233	29.4		378	45.1	611	38.7
≥ 35		44	47.3		132	58.3	176	53.5
p for linear trend[†]			**			***		***
p for gender difference				***				
p for gender*BMI interaction				*				
Waist circumference (m)		n = 1 067	%		n = 1 565	%	n = 2 632	%
I	M: 0.72–0.925 W: 0.59–0.835	253	20.6		390	29.7	643	25.8
II	M: 0.93–0.995 W: 0.84–0.92	281	16.8		404	30.6	685	24.8
III	M: 1.00–1.07 W: 0.925–1.00	265	23.5		372	36.5	637	31.2
IV	M: 1.075–1.49 W: 1.005–1.62	268	33.2		399	50.7	667	43.5
p for linear trend			***			***		***
p for gender difference				***				
p for gender*waist circumference interaction				0.602				
Body fat percentage (%)		n = 905	%		n = 1 219	%	n = 2 124	%
I	M: 9.3–20.8 W: 13.9–31.4	224	8.4		295	23.2	519	16.5
II	M: 20.9–25.0 W: 31.5–35.6	222	15.3		303	21.0	525	18.1
III	M: 25.1–29.1 W: 35.7–40.0	229	16.8		312	32.1	541	25.3
IV	M: 29.2–44.6 W: 40.1–56.6	230	31.5		309	45.5	539	39.1
p for linear trend			***			***		***
p for gender difference				***				
p for gender*body fat percentage interaction				0.100				

Continued overleaf

Table 4 continued

	Men [1]			Women [1]		Total [1,2]	
Obesity history	n = 877	%		n = 1 157	%	n = 2 034	%
Never obese	612	15.2		748	22.7	1360	19.3
Previously obese, currently non-obese	39	26.3		32	47.5	71	36.8
Currently obese, but non-obese at ages 20–50	151	23.9		285	37.0	436	31.2
Obese since age 50 years	47	26.3		67	53.7	114	42.5
Obese since age 40 years	18	36.5		21	59.0	39	49.0
Obese since age 30 years	10	44.5		4	69.6	14	56.9
p for linear trend [‡]		*			**		***
p for gender difference			***				
p for gender*obesity history interaction			0.603				

Notes: The data in this table are limited to subjects who had not lost unintentionally more than 5 kg in weight during the previous 12 months. [1]Adjusted for age. [2]Adjusted for gender. [†]Underweight persons were not included in the linearity analysis. [‡]Previously obese, but currently non-obese persons were not included in the linearity analysis. *** p < 0.0001, ** p < 0.01, * p < 0.05.

5.3 Mediating factors between obesity and walking limitation (I, II)

In order to study the mediating role of obesity-related diseases between high BMI and walking limitation, sequential logistic regression analyses were performed. The age-adjusted models indicated that the risk of walking limitation was statistically significantly increased among obese and severely obese men, and in overweight, obese, and severely obese women (Table 5). After adjusting for education, marital status and smoking, the ORs in men remained rather similar (7% decrease in OR among severely obese men), and were attenuated somewhat more in women (14% in overweight, 15% in obese, and 19% in severely obese). Adjusting further for chronic diseases substantially reduced the ORs in men (60% in obese and 46% in severely obese) and women (40% in overweight, 45% in obese, and 45% in severely obese). However, the excess risk of walking limitation remained statistically significant in severely obese men (OR 2.78, 95% CI 1.30–2.78), and in obese (OR 1.97, 95% CI 1.38–2.81) and severely obese women (OR 3.64, 95% CI 2.12–6.26). Of all the chronic diseases, type 2 diabetes in men (32%) and knee osteoarthritis in women (18%) contributed most to the association between high BMI and walking limitation, followed by hypertension in men (14%) and angina pectoris in women (8%). The changes in the log likelihood scores indicate that the adjusted variables contributed slightly more to the association between BMI and walking limitation in men than in women.

Table 5. ***The risk of walking limitation in different body mass index categories and the effect of mediating factors for men and for women***

	Men			Women		
	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Body mass index						
18.5–24.9	1.00	1.00	1.00	1.00	1.00	1.00
25–29.9	0.97 (0.66–1.42)	1.05 (0.71–1.57)	0.91 (0.60–1.37)	1.47 (1.10–1.96)	1.40 (1.03–1.91)	1.28 (0.93–1.76)
30–34.9	1.63 (1.04–2.55)	1.65 (1.03–2.65)	1.25 (0.76–2.05)	2.77 (2.01–3.82)	2.50 (1.80–3.49)	1.97 (1.38–2.81)
≥ 35	4.33 (2.20–8.53)	4.10 (2.01–8.38)	2.78 (1.30–5.95)	5.80 (3.52–9.54)	4.91 (2.95–8.15)	3.64 (2.12–6.26)
Age, years	1.13 (1.11–1.16)	1.12 (1.10–1.15)	1.11 (1.08–1.14)	1.16 (1.14–1.17)	1.14 (1.13–1.16)	1.12 (1.10–1.14)
Education						
Basic		3.62 (2.00–6.55)	3.13 (1.68–5.84)		2.92 (2.01–4.23)	2.63 (1.80–3.86)
Intermediate		2.18 (1.26–3.78)	1.98 (1.10–3.58)		1.99 (1.38–2.87)	1.80 (1.22–2.65)
Higher		1.00	1.00		1.00	1.00
Living alone*		2.12 (1.47–3.06)	2.45 (1.67–3.59)		1.38 (1.10–1.75)	1.38 (1.08–1.77)
Current smoking[†]		1.65 (1.14–2.40)	1.64 (1.11–2.40)		1.47 (1.08–2.00)	1.54 (1.11–2.13)
Angina pectoris			1.24 (0.84–1.84)			1.89 (1.36–2.62)
Heart failure			3.02 (1.54–5.92)			2.22 (1.26–3.93)
Hypertension			1.38 (0.96–1.99)			1.14 (0.88–1.48)
Type 2 diabetes			2.78 (1.72–4.50)			1.52 (0.97–2.39)
Knee osteoarthritis			1.67 (1.02–2.74)			1.87 (1.37–2.55)
Hip osteoarthritis			2.28 (1.39–3.71)			2.18 (1.36–3.49)
-2 Log L	1052.63	991.67	932.21	1560.41	1511.43	1438.28

Notes: Model 1: adjusted for age; Model 2: Model 1 + adjustment for education, marital status, and smoking; Model 3: Model 2 + adjustment for angina pectoris, heart failure, hypertension, type 2 diabetes, knee and hip osteoarthritis. *Reference for living alone (divorced, separated, widowed, or single) is married or cohabiting. [†]Reference for current smoking is non-smoking (never or ex-smoker). OR = odds ratio; CI = confidence interval; -2 Log L = Log likelihood score indicates model fit.

By limiting the study population to those persons, who participated in the health examination, it was possible to conduct a more detailed analysis on the potential mediators between obesity and walking limitation. In addition to chronic diseases, the mediating role of biological indicators, CRP and handgrip strength, known to be associated with obesity and functional limitation, were studied. First, the independent associations between BMI, waist circumference, and body fat percentage, CRP, handgrip strength, and walking speed were studied with linear regression analyses. After adjustment for potential confounders (age, gender, education, smoking, alcohol use, coronary heart disease, hypertension, pulmonary disease, type 2 diabetes, arthritic disease, anti-inflammatory drugs and estrogen use), high BMI, high waist circumference, and high body fat percentage were positively associated with higher CRP (p for all < 0.0001). Moreover, negative and statistically significant associations were found between CRP and handgrip strength ($p = 0.001$) and CRP and walking speed ($p < 0.0001$). In addition, handgrip strength was positively associated with walking speed ($p < 0.0001$).

Logistic regression analysis was used to study the mediating factors between body fat percentage and walking limitation (Figure 5). After controlling for education, health behavioral factors (smoking and alcohol use), several chronic diseases (coronary heart disease, hypertension, pulmonary disease, type 2 diabetes, and joint disease), and use of anti-inflammatory drugs and estrogen, the ORs for the lowest to the highest body fat percentage quartiles were 1.0 (reference), 1.20 (95% CI 0.78–1.83), 1.80 (95% CI 1.23–2.67), and 3.10 (95% CI 2.13–4.52), respectively. Further adjustment for CRP attenuated greatly the ORs in body fat percentage quartiles III and IV. Finally, adjusting additionally for handgrip strength and body height reduced further the effect of fat percentage on walking limitation. In the final model, the excess prevalence of walking limitation in the two highest quartiles for body fat percentage remained statistically significant, the ORs being 1.64 (95% CI 1.11–2.44) and 2.53 (95% CI 1.70–3.77), respectively. In the gender-specific analyses, CRP and handgrip strength attenuated the association between body fat percentage and walking limitation more in women than in men. The respective percentage reductions in women and men were 30% and 17% for CRP and 15% and 7% for handgrip strength. There was a significant interaction effect of gender*handgrip strength on walking limitation in the two highest quartiles for body fat percentage ($p = 0.04$ and $p = 0.02$).

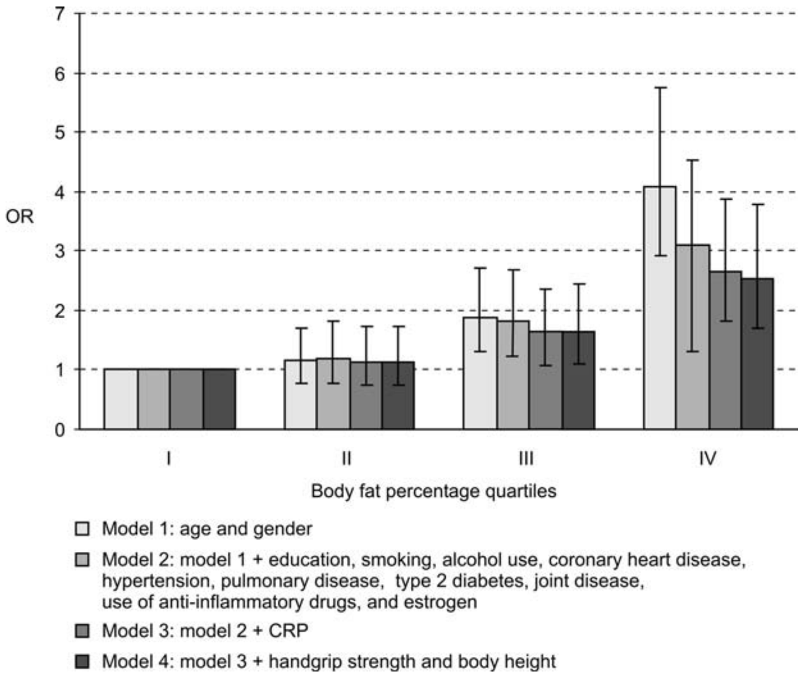

Figure 5. ***Effects of different groups of mediators on the risk of walking limitation in body fat percentage quartiles.***

5.4 Long-term risk of walking limitation in relation to obesity and physical impairments (III, IV)

In a retrospective longitudinal study, in addition to current obesity, early onset of obesity and obesity duration were found to increase the risk of walking limitation. An increasing gradient in the age- and gender-adjusted risk of walking limitation from never obese, through currently obese, to obese since age 50, 40, and age 30 years was found (*p* for linear trend < 0.0001) and the corresponding ORs and 95% CIs were 1.00, 2.29 (1.70–3.09), 4.33 (2.59–7.23), 6.01 (2.55–14.14), and 8.97 (3.06–26.29). The risk of walking limitation was also significantly higher among those who were currently non-obese but had previously been obese (OR 3.15, 95% CI 1.63–6.11). This was the only obesity history category where the increased risk of walking limitation did not remain statistically significant after adjusting for education, life style factors and chronic diseases. The impact of chronic diseases was particularly prominent in this group of previously obese but currently non-obese persons, largely explaining the high risk of walking limitation.

A negative effect of midlife obesity on walking limitation was found in the Mini-Finland Follow-up Survey, where persons were followed for 22 years. Among the 840 persons who did not initially have walking limitation, walking limitation developed over the 22-year follow-up in 176 subjects. The age-adjusted incidence of walking limitation was higher among women (25%) than men (16%) ($p < 0.0001$). The prevalence of obesity in 1978–1980 was relatively low (5.2% in men and 11.1% in women), but the age- and gender-adjusted risk of later life walking limitation was higher among initially obese persons (OR 3.57, 95% CI 1.93–6.62) compared with normal weight persons. Furthermore, the risk of later life walking limitation per standard deviation (SD) increase in BMI was significant (OR 1.39, 95% CI 1.10–1.75) after adjustment for baseline confounders (age, gender, education, physical activity, alcohol use, smoking, angina pectoris, heart failure, hypertension, chronic bronchitis, diabetes, low back syndrome, and knee osteoarthritis). In addition to obesity, physical impairments (low handgrip strength, running and squatting difficulties) in middle age predicted later life walking limitation, and the associations remained significant after adjusting for baseline confounders. The adjusted risk of walking limitation was 2.4-fold among those who had major running difficulties and 4.6-fold among those who had squatting difficulties compared with those who had no difficulties. The corresponding OR for handgrip strength was 0.56 (95% CI 0.38–0.81) per an increment of one SD.

5.5 The effect of coimpairment and comorbidity on walking limitation (I, II, IV)

At the baseline of the Mini-Finland Follow-up Survey, the prevalence of diseases was relatively low. Therefore the effect of coimpairment, instead of comorbidity, on later life walking limitation was studied. Coimpairment was defined according to the combination of overweight and physical impairments, and altogether six categories were produced (Figure 6). The age- and gender-adjusted risk of walking limitation was over six times higher among those who were overweight (highest BMI tertile) and had two or more physical impairments as compared with those who were neither overweight nor had impairments (OR 6.35, 95% CI 2.82–14.33). Also those subjects who were not overweight but had two or more physical impairments had an over five-fold higher risk of walking limitation (OR 5.42, 95% CI 2.57–11.42). No interaction effect of overweight*number of physical impairments on walking limitation was found.

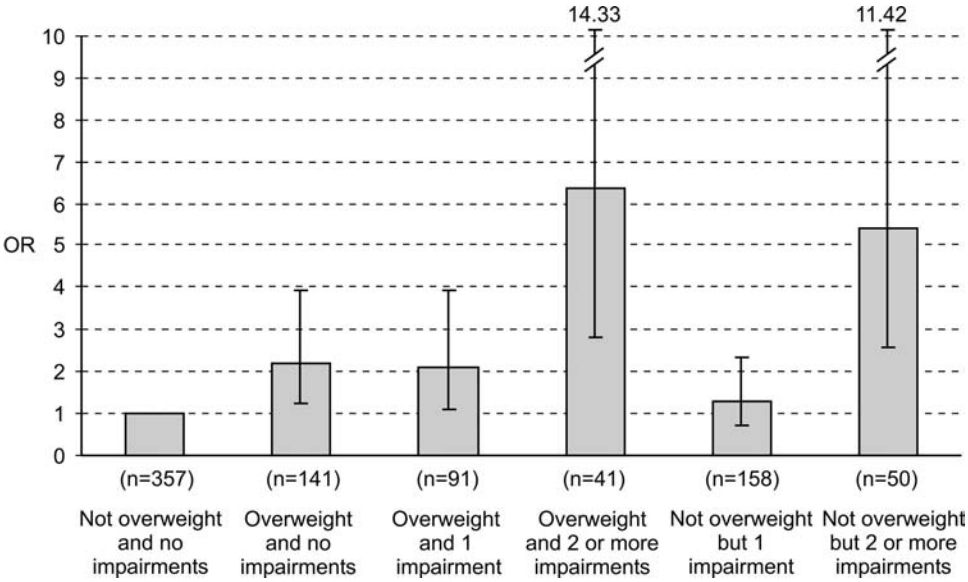

Figure 6. ***Age- and gender-adjusted risk of walking limitation according to number of physical impairments with or without coexisting overweight at baseline. Overweight is defined as the highest BMI tertile.***

In the Health 2000 Survey, the effect of comorbidity on walking limitation was evaluated by categorizing subjects into six categories according to their obesity and disease status (Figure 7). The age- and gender-adjusted risk of walking limitation was over 6.5 times higher among those who were obese (BMI ≥ 30 kg/m^2) and had two or more diseases as compared with those who neither were obese nor had diseases (OR 6.51, 95% CI 4.76–8.90). Also those subjects who were not obese but had two or more diseases had an over three-fold higher risk of walking limitation (OR 3.22, 95% CI 2.48–4.18). No interaction effect of obesity*number of diseases on walking limitation was found.

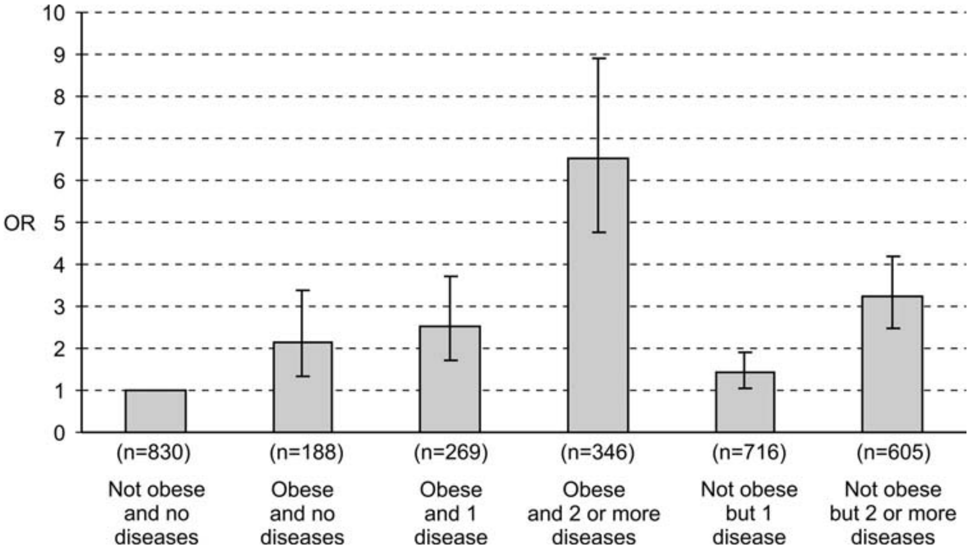

Figure 7. ***Age- and gender-adjusted risk of walking limitation according to number of diseases with or without coexisting obesity. Obesity is defined as BMI ≥ 30 kg/m^2.***

Finally, the cross-sectional data were used to identify the most vulnerable persons in terms of obesity and handgrip strength and to study the effect of the combination of high body fat percentage and low handgrip strength on walking limitation. A clear gradient of increased prevalence of walking limitation with decreasing handgrip strength was found within all three body fat percentage categories (Figure 8). Among those with both low handgrip strength and high body fat percentage, the prevalence of walking limitation was 61%, whereas in the group with high handgrip strength and low body fat percentage only 7% had walking limitation. No interaction effect of fat percentage*handgrip strength on walking limitation was found.

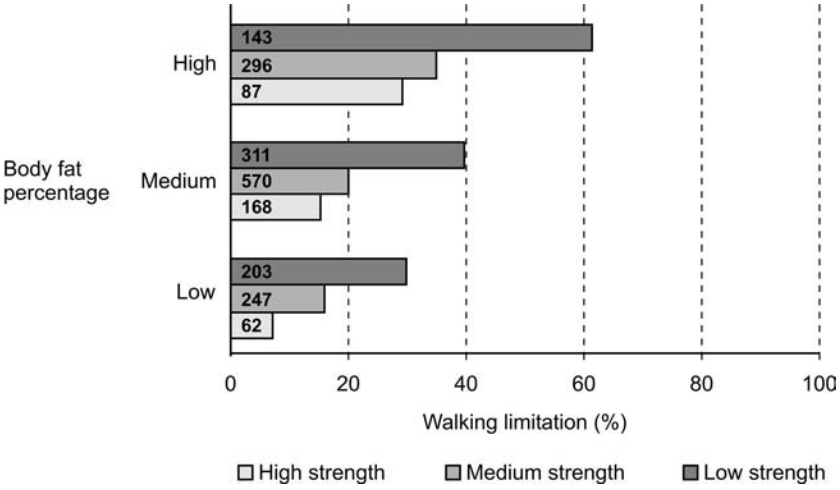

Figure 8. *The age- and gender-adjusted prevalence of walking limitation according to body fat percentage levels and handgrip strength. Low, medium and high levels of fat percentage and handgrip strength were defined by combining quartiles II and III. Numbers inside the bars indicate the number of persons in each category.*

6 DISCUSSION

In this study of a representative population-based sample of Finnish men and women aged 55 years or older, overweight and obesity were found to be independently associated with walking limitation, more strongly in women than in men. The factors that contributed most to the association between BMI and walking limitation were type 2 diabetes in men and knee osteoarthritis in women. In addition, adjusting for CRP and handgrip strength attenuated the association between high body fat percentage and walking limitation. This study also showed that high BMI measured in middle age predicted walking limitation 22 years later. Similarly, simple tests of physical impairments were found to be predictive of later life walking limitation. In addition to midlife obesity, duration of obesity over several decades also increased the risk of walking limitation. Finally, the present study demonstrated that overweight or obese persons with coexisting diseases or physical impairments comprise a high risk group with regard to current or future walking limitation compared with only overweight or obese persons, indicating that comorbidity and coimpairment have a negative effect on physical functioning.

6.1 Obesity and walking limitation: mediating factors, long-term risk and coexisting conditions

Association between different obesity indicators and walking limitation

Consistent with previous cross-sectional population-based studies, high BMI (Coakley et al. 1998; Davison et al. 2002; Larrieu et al. 2004; Ramsay et al. 2006), large waist circumference (Ramsay et al. 2006), and high body fat percentage (Visser et al. 1998a; Visser et al. 1998b; Broadwin et al. 2001; Sternfeld et al. 2002; Ramsay et al. 2006) were all found to be strongly associated with an increased prevalence of walking limitation after controlling for medical conditions and several other covariates. Only one other study was found in which these three obesity indicators have been studied simultaneously as determinants of walking limitation and compared with each other (Ramsay et al. 2006). In their study of older British men, Ramsay et al. (2006) compared obesity indicators and their association with walking limitation with ROC analyses, and found that the areas under the curve were similar for BMI, waist circumference, and body fat mass index. Their finding is in accordance with the results of the present study showing that BMI, waist circumference and body fat percentage all identify persons at risk of walking limitation.

However, the differences between BMI, waist circumference, and body fat mass as measures of obesity in older adults deserve to be discussed. In health-related research, BMI is a more commonly used measure of obesity than waist circumference or body fat percentage, and it has well-established and internationally accepted cut-off points (World Health Organization 2000; Zamboni et al. 2005). Although BMI is a good indicator of general obesity, it does not give information about fat distribution and does not differentiate between fat and muscle mass. Consequently, it may underestimate adiposity among older persons who, because of age-related loss in lean body mass, have a greater amount of body fat than younger people with a similar BMI (Prentice and Jebb 2001). In addition to changes in body composition, age-related decline in body height may modify BMI (Sorkin et al. 1999). Thus, aging has an increasing influence on the numerator and decreasing influence on the denominator of BMI (Zamboni et al. 2005).

Waist circumference, in turn, is a surrogate of abdominal obesity and strongly associated with visceral fat when measured with MRI (Stewart et al. 2003). Although body fat percentage and other indicators of body fatness can be measured objectively with BIA, DXA, CT or other sophisticated measures, they are not a realistic means of identifying at risk individuals in routine primary health care. Therefore, to achieve reliable information about obesity in older persons, it has been suggested that waist circumference could be used as a complementary measurement in addition to BMI (Zamboni et al. 2005). Waist circumference may be particularly useful when a reliable measure of weight and height for making BMI calculations cannot be obtained. However, interpreting waist circumference values is not an unequivocal in older persons. Due to loss of height and kyphotic stature, there is a decrease in the vertical space of the abdominal cavity and the diaphragm moves downwards causing waist circumference to increase.

Mediating factors between obesity and walking limitation

Relatively little research has been performed to explain the possible mediators between obesity and walking limitation including sociodemographic and health behavioral factors, chronic diseases and biological indicators. According to this study, the association between obesity and walking limitation was more pronounced in women than in men, an increased risk being observed for overweight women, whereas in men only obesity and severe obesity were significantly associated with walking limitation. This gender difference has also been found in other studies based on self-reported mobility limitation or disability (Friedmann et al. 2001; Davison et al. 2002; Larrieu et al. 2004; Angleman et al. 2006). Friedmann and coworkers (2001) have discussed potential explanations for the gender difference, such as differences in disabling conditions and differences in reporting physical discomfort (Merrill et al. 1997). An additional explanation may relate to body composition. Women have more fat as well as lower absolute and relative muscle strength than men (Visser et al. 2002a; Lafortuna et al. 2005), and thus they may have more difficulties in bearing their excess weight and in moving efficiently. Women, compared to men, also more commonly have lower aerobic capacity (Fleg et al. 2005) and they are physically less active (DiPietro 2001), thus predisposing older obese women, in particularly, to walking limitation. Finally, the gender difference in survival may have its own effect on the association in question (Jensen 2005), as obese men may die before to emerging functional limitation, whereas women are known to live longer with functional limitations and disabilities (Leveille et al. 2000).

In addition to gender differences in the association between obesity and walking limitation, the results of this study suggest that different diseases may mediate the effect of obesity on walking limitation. In men, the strong role of type 2 diabetes is probably due to the fact that in the older obese population type 2 diabetes is more prevalent among men than among women (Must et al. 1999). The potential pathways through which diabetes may affect walking limitation include diabetes-related complications such as sensory-motor neuropathy, peripheral vascular disease, and visual impairment (Nathan 1993; Al Snih et al. 2005). In addition, insulin resistance may have a negative effect on walking through decline in muscle mass and strength (Abbatecola et al. 2005; Guillet and Boirie 2005). The relatively strong effect of knee osteoarthritis on walking limitation among overweight or obese women found in this study may reflect the fact that excess body weight causes mechanical stress on the patellofemoral joint, and the consequent pain and impaired muscle strength predispose women to walking limitation (Ling et al. 2003; Messier et al. 2005). In addition, female gender and overweight are both strong risk factors for knee osteoarthritis (Felson et al. 2000). Osteoarthritis, in turn, is a risk factor for mobility limitation (Clark and Mungai 1997; Ling et al. 2003).

The present study is among the first to examine obesity, CRP, handgrip strength, and walking limitation simultaneously, thereby allowing more detailed examination of the complex mechanisms around obesity and walking limitation. The results suggest that in addition to obesity-related diseases, low-grade inflammation through cytokine production in adipose tissue and decreased muscle strength due to accelerated catabolism in muscle may partially explain the pathway from obesity to walking limitation. Although no other corresponding studies are available, some recent studies have investigated the associations between obesity, inflammatory markers, muscle mass or strength (Pedersen et al. 2003; Cesari et al. 2005b; Schrager et al. 2007), and frailty (Blaum et al. 2005). In studies related to muscle mass and strength, inflammatory markers were found to be positively associated with obesity and negatively with high lean body mass or muscle strength, supporting the findings of the present study. In contrast, in a study of older women, CRP was not found to be associated with frailty among obese persons (Blaum et al. 2005). However, it needs to be emphasized that although CRP was found to be a significant explanatory factor between high body fat percentage and walking limitation in this study, CRP itself may not be the biologically relevant molecule mediating the effect of obesity on walking limitation. Rather, CRP may serve as a marker for the upregulation of the inflammation pathway and other inflammatory markers such as TNF-α and IL-6. Several studies have shown an association between TNF-α and IL-6 and decreased muscle strength (Visser et al. 2002b; Schaap et al. 2006) as well as mobility limitation (Cesari et al. 2004; Penninx et al. 2004; Figaro et al. 2006).

In addition to obesity-related low-grade inflammation, muscle strength may decrease because of an increased level of fat infiltrated in the muscle, which is common among people with high overall body fatness (Ryan and Nicklas 1999). Indeed, there is evidence that fat infiltration into muscle is associated with lower muscle strength and walking performance (Sipilä and Suominen 1994; Goodpaster et al. 2001; Visser et al. 2005), thus supporting the pathway from obesity through decreased muscle strength to walking limitation. In concordance with that hypothesis, the present study found that persons with a high body fat percentage and low muscle strength had a substantially higher risk of walking limitation than either obese or weak persons. A few studies on sarcopenic obesity and functional limitation exists, and Baumgartner et al. (2000; 2004) have reported similar results. However, the combination of high fat percentage and low muscle strength used in this study differs slightly from the concept of sarcopenic obesity in which sarcopenia refers to low muscle mass. According to present knowledge, in older persons muscle strength may be a more important predictor in terms of mobility and physical functional capacity than muscle mass (Visser et al. 2000; Visser et al. 2005). Although the loss of muscle strength with aging is mainly due to decreased muscle mass, strength is often reduced to a greater degree than muscle mass (Goodpaster et al. 2006). This indicates that there may be other factors, such as reduced motor unit activation (Jakobi and Rice 2002) or reduced muscle quality (Visser et al. 2005) which also contribute to the loss of strength.

A potential mediating factor that was not included in the analyses in studies I and II is physical activity. It is known that physical activity is an important determinant of physical functional capacity in older persons, and also that physical inactivity and obesity are related (Bernstein et al. 2004; Brach et al. 2004b; Di Francesco et al. 2005). However, in gerontological research the role of physical activity in the association between obesity and walking limitation is complicated, especially if studied with cross-sectional data. It is obvious that having walking limitation will also reduce physical activity, and therefore studying both of these factors simultaneously may introduce bias into the results. In contrast, in a longitudinal setting, it is clear that physical activity plays a major role in the vicious circle of obesity, muscle strength, and walking limitation. A sedentary lifestyle decreases physical performance and also exposes to an increase in adipose tissue. This in turn may increase the level of circulating inflammation markers and predispose to several diseases, thus decreasing muscle mass and strength, and further impairing walking and decreasing physical activity. Physical inactivity is thus closely connected to the factors that were identified in the present study as mediators in the association between obesity and walking limitation. Although physical activity level was not controlled in the cross-sectional studies (I and II), handgrip strength and other covariates may have conveyed some of the effects of physical activity on the relationship between obesity and walking limitation.

Physical activity has a crucial role in reversing the above-described negative chain of causation. First, physical activity can facilitate weight loss and weight maintenance (Fogelholm and Kukkonen-Harjula 2000; Ross and Janssen 2001; Jakicic et al. 2003). Second, physical activity has been found to be associated with a lower level of inflammatory markers (Reuben et al. 2003; Colbert et al. 2004), to improve muscle strength and aerobic capacity (Keysor and Jette 2001; Latham et al. 2003), and to have positive impact on several diseases such as type 2 diabetes and cardiovascular diseases (Hu et al. 2004; Lakka and Laaksonen 2007). Moreover, studies examining the combined effect of obesity and physical activity have shown that the negative health effects related to obesity can be attenuated by physical activity. For example, He and Barker (2004) found that regular exercise significantly reduced the risk of developing mobility limitation among obese individuals.

Long-term risk of obesity and weight loss

There are few studies on the early risk factors of walking limitation. However, it is important to study further this topic in order to recognize persons at risk of adverse health outcomes in the future. The present study was among the first to show the long-term risks of obesity on later life walking. It was also found that physical impairments in middle-aged people predict walking limitation in older age. The findings are valuable and confirm the results obtained from earlier studies on the effect of obesity (Launer et al. 1994; Ebrahim et al. 2000; Houston et al. 2005b), muscle strength (Rantanen et al. 1999b; Rantanen et al. 2000) and certain diseases, such as osteoarthritis (Guralnik and Kaplan 1989; Hubert et al. 1993; Ettinger et al. 1994), back pain (Guralnik and Kaplan 1989) and hypertension (Pinsky et al. 1985;

Guralnik and Kaplan 1989; Keil et al. 1989; Lammi et al. 1989), on functional capacity. The results of this study further supports the claim that the basis for good functional capacity in old age is built earlier in life. Thus, increasing physical fitness through physical activity and the promotion of weight loss in overweight middle-aged persons may prevent mobility limitation and subsequent disability in old age.

Even modest weight loss among obese people of working age has many positive effects on the risk factors for coronary heart disease and type 2 diabetes through lowering blood pressure and improving the metabolic profile (National Institutes of Health 1998; Ross et al. 2004). In addition, weight loss has been found to alleviate pain in people with knee osteoarthritis (Huang et al. 2000; Martin et al. 2001) and improve physical function and health-related quality of life (Fine et al. 1999; Kaukua et al. 2003). However, weight loss attempts in old age may have adverse effects on health and functional capacity. So far, a few studies on the effects of intentional weight loss on obese elderly people's health and functional capacity have been published. In those studies, depending on the interventions and outcome measures used, conflicting results have been obtained (French et al. 1995; Messier et al. 2004; Lee et al. 2005; Messier et al. 2005; Villareal et al. 2006). It has been suggested that a supervised weight loss program, which includes physical exercise and possibly vitamin D and calcium supplements may help to maintain muscle mass and bone mineral density, should be relatively safe for older obese persons (Newman et al. 2005; Zamboni et al. 2005; Villareal et al. 2006).

Distinguishing between intentional and unintentional weight loss in older people is important, as their effects on health and functional capacity may be different and they stem from different backgrounds. Intentional weight loss is often due to life style modifications such as increased physical activity and/or decreased energy intake, whereas unintentional weight loss often reflects frailty (Fried et al. 2001b), severe diseases, underlying inflammatory process, insufficient nutritional intake or depressive symptoms (Wannamethee et al. 2000; Bales and Ritchie 2002). There is evidence that unintentional weight loss as well as another indicator of poor nutritional status in old age, underweight (BMI < 18.5 kg/m^2), are associated with poor mobility (Davison et al. 2002; Larrieu et al. 2004) and predict subsequent functional limitation, disability, and mortality (French et al. 1999; Ferraro et al. 2002; Lee et al. 2005; Mendes de Leon et al. 2006). Although the risk of underweight increases with aging (Thompson Martin et al. 2006) and is an important determinant of functional capacity, it was not possible to examine the association between underweight and walking limitation in the present study, because there were so few underweight persons in the sample. Respectively, due to the J-shaped association between BMI and functional limitation in old age, there was no justification for including underweight persons in the normal weight category. Therefore, in studies I–III underweight subjects were excluded from the analyses.

Similarly, subjects who had unintentionally lost weight (more than 10 kg in study I and more than 5 kg in studies II and III) during the past year were excluded from the analyses.

Obesity, coexisting conditions and walking limitation

The results of the present study indicate for the first time that obesity and coexisting diseases increase the risk of walking limitation and that overweight and coexisting physical impairments in middle-aged people predict later life walking limitation. These findings are in concordance with earlier studies which have reported a negative effect of excess body weight and coexisting physical impairment and disease on health outcomes (Ettinger et al. 1994; Rantanen et al. 2000). These results also show that obese persons are a heterogeneous group, which includes those who have diseases or physical impairments and those who are obese, but have no other diseases or physical impairments. Because obese persons with comorbidities or coimpairments are at substantially higher risk of walking limitation than obese persons with neither of these conditions, individuals with excess body weight should be carefully screened in health care for obesity-related diseases, as well as for physical impairments.

From the preventive point of view, it is important to develop and evaluate proper interventions to decrease the risk of walking limitation due to comorbidities and coimpairments. Since the increased risk of walking limitation is a consequence of obesity and coexisting conditions, it is reasonable to assume that interventions aiming either to reduce excess body weight or to alleviate diseases or physical impairments are likely to reduce the risk of walking limitation. If this is the case, overweight middle-aged persons might greatly benefit not only from weight loss but also from physical exercise -related interventions designed to improve e.g. muscle strength or aerobic capacity. Furthermore, management of obesity-related diseases among older persons may prevent or reduce walking limitation associated with obesity. However, longitudinal studies and clinical trials are needed to verify these hypotheses related to coimpairment and comorbidity.

6.2 Methodological considerations

Study samples and designs

The major strength of the present study is the used data sets. The Health 2000 Survey is one of the few comprehensive national health interview and examination surveys that exist in the world. The data are representative of the entire adult population in Finland and allow good generalizability of the results. A representative population-based data set has several strengths over clinical samples and studies on volunteers. First, a representative sample includes both men and women from different age-groups and different residential locations as well as healthy and diseased individuals. Secondly, if the sampling is based on population register data, as it was in the Health 2000 Survey, all individuals with similar basic demographic data (age, gender, residential location) have an equal chance of inclusion in the sample independently of their health or socioeconomic status.

In order to obtain reliable results in a representative population-based study the individuals selected should participate in the study. In the Health 2000 Survey, a high participation rate (94%) was achieved, indicating that the findings would have high external validity. Several efforts were made to increase the willingness to participate, e.g. information campaigns, abbreviated health examinations at home or in institutions, an abbreviated telephone interview and a mailed questionnaire for those who did not participate in the study center or home examination, as well as the use of proxy respondents if the individual was not able to participate otherwise in the interview (2.6%, n = 78). There is evidence that non-participants often differ from participants in terms of age, health behavior and health status (Goldberg et al. 2001; Jousilahti et al. 2005). Typically non-respondents are older, more diseased and disabled, and thus may be underrepresented such a study as the present one. However, because the participation rate was very high in this study, selective non-participation is not likely to have markedly biased the results.

In addition to a representative sample and high participation rate, to obtain reliable results from population-based studies, the sample has to be large enough. In the Health 2000 Survey power calculations were performed and after taking financial and temporal constraints into consideration, a sample of 8 028 persons was obtained. A two-staged stratified cluster sample was used to facilitate the organization and cost-effectiveness of the implementation of health examinations in the study municipalities, which were scattered around Finland. Despite the long distances between municipalities in the northern part of the country, good transportation links enable large-scale nationwide studies to be conducted in Finland. In contrast in, for example, the United States, the implementation of a reliable national health examination survey is far more difficult and expensive.

The data set used in Study IV, the Mini-Finland Follow-up Survey, is also internationally unprecedented due to 22-year follow-up period and the use of a health examination at both baseline and follow-up. Non-participation is particularly common in longitudinal studies, because people move out the area; die, or are unable to participate due to poor health status (Goldberg et al. 2006). In the Mini-Finland Follow-up Survey, only 12% of the eligible survivors of the Mini-Finland Health Examination Survey were lost to the follow-up. These persons were older, had higher BMI, lower handgrip strength, and more medical conditions at the baseline in comparison to those who participated in the follow-up phase of the study. In addition, the prevalence of difficulties in squatting and running 500 meters at the baseline was higher among the drop-outs than follow-up participants. The follow-up participants were therefore leaner and showed better physical performance than non-participants; thus the associations of BMI and physical impairments with walking limitation reported in this study are likely to be conservative rather than overestimated. Because large municipalities only were selected for the follow-up examination and since a substantial proportion of the initial cohort had died during 22-year interval, it was not possible to control for the effects of selection on the invitation to the follow-up in the present study.

General validity and reliability aspects

To obtain reliable results, the methods and instruments used in a survey should be valid and repeatable. In the Health 2000 Survey, a health interview was implemented by trained interviewers from Statistics Finland and a health examination by trained professionals and calibrated instruments. To ensure the validity and repeatability of the measurements, written instructions were issued and a thorough training was organized before the study. During the data collection phase, the quality of the measurements was monitored with observations and repeated measurements. The reliabilities of the physical performance measures of handgrip strength and walking speed were excellent and moderately good, respectively. The reliability of the waist circumference measurement was excellent. The reliability of the questionnaires was improved by checking that the returned questionnaires had been properly filled in before acceptance at the examination site and by helping the subjects to fill in the missing answers whenever possible.

Impaired cognitive status is one factor that may decrease the reliability of the results (Blaum et al. 2002). However, in this study all persons regardless of their cognitive status were included in the analyses. In the Health 2000 Survey, cognitive function was examined with an abbreviated Mini-Mental State Examination (MMSE) with a maximum score of 16 points (Folstein et al. 1975). Eleven percent of the participants aged 55 years and over had a value below 11 points. The majority of these persons received 9 or 10 points in the test, suggesting mild cognitive decline. The outcome measure of this study, maximum walking speed over 6.1 meters, represents a routine physical task which should not be substantially affected by a mild cognitive deficit. As the person responsible for carrying out the tests observed that each participant performed the test in an acceptable manner, there is no reason to believe that the results are substantially affected by cognitive status. Furthermore, the tests were not performed for those six persons who were apparently unable to understand the instructions, even though a specific MMSE score cut-off points was not used as an exclusion criterion.

Walking limitation

In this study walking limitation served as the outcome variable, and it was based primarily on walking speed. The cut-off point for a walking speed indicative of walking limitation was chosen according to the ROC analysis. The analysis showed that 1.2 m/s had the greatest diagnostic accuracy of self-reported walking difficulty in walking 500 meters. In addition, the chosen speed also served as a proxy for the ability to cross a street safely at light-controlled intersection, if crossing starts at the moment when the green light for pedestrians goes out (pedestrian protection time), as is the case in Finland and the United States (LIVASU-95 1996; Langlois et al. 1997). In other studies, several walking speed cut-off points have been used depending on the target group and on the way the walking test has been performed, e.g. walking with usual or with maximal speed. In the Women's Health and Aging Study (e.g. Rantanen et al. 1999a) and in the Established Populations for Epidemiologic Studies of the Elderly (e.g. Guralnik et al. 1995) a cut-off of 0.4 m/s at usual walking speed was used to indicate severe walking disability, and was later found to predict subsequent disability (Guralnik et al. 2000). In the Health, Aging and Body Composition Study a usual walking speed of less than 1.0 m/s was used and found to be predictive of persistent lower extremity limitation, hospitalization, and death (Cesari et al. 2005a). Also Studenski et al. (2003) used a cut-off point of 1.0 m/s and found it to predict decline in function and health. In fact, if usual walking speed represents a level of performance of about 70–80% of maximal speed, the speed of 1.2 m/s used in this study would correspond quite well with the speed used in the Health, Aging and Body Composition Study, making possible to compare the results.

In this study as well as in the above-mentioned studies, the cut-off point for walking speed was the same for the whole study population. However, walking speed is partially explained by gender and body height and therefore men and taller persons tend to walk faster than women and shorter persons. Although height-normalized values for walking speed have been presented separately for men and women as well as for different age-groups (Bohannon 1997), in real life traffic lights do not take into account the gender or age of pedestrians. Thus, each person regardless of age, gender or height has to be able to walk at a standard speed in order to cross the streets safely.

By combining the information on low walking speed and self-reported walking difficulty, it was possible to obtain a more representative picture of the variation of walking limitation in the Finnish population. Using walking speed alone as an indicator of impaired mobility would have resulted in the exclusion of a number of people with walking limitation, because many of the most severely disabled and diseased persons were either not able or unwilling to take part in the measurements (Sainio et al. 2006). Although performance-based tests and self-reported difficulties provide partially discordant results (Guralnik et al. 2000; Simonsick et al. 2001b; Ferrucci et al. 2004), the current opinion in gerontological research is that these measures of physical functioning should be used as complementary measures (Guralnik et al. 1994; Cress et al. 1995; Sakari-Rantala et al. 2002). Consequently, several studies have been published in which a combination of performance-based tests and self-reports in walking have been used (Rantanen et al. 1999a; Reuben et al. 2004). In addition to walking, the information regarding medical conditions was also mainly based on a clinical examination by a physician, but supplemented with self-reports in studies I and III (21% and 25%). In studies II and IV, only clinical diagnoses were used.

Obesity indicators

In this study, the majority of the analyses were performed using BMI as the measure of obesity. Information on BMI was obtained from a larger population (n = 2 895) than waist circumference (n = 2 632) or body fat percentage (n = 2 124). In addition, among these measures BMI is the only one which has internationally accepted and widely used cut-off points to indicate risk of ill health (World Health Organization 2000). Categorizing different levels of obesity enables meaningful comparisons of weight status within and between populations, and the identification of individuals and groups at increased risk of adverse health or functional outcomes (World Health Organization 2000). However, in study II body fat percentage was mainly used, because in that study special emphasis was placed on low-grade inflammation, and adipose tissue has been reported to be an important source of inflammatory markers (Mohamed-Ali et al. 1997).

The obesity measures used in this study were mainly based on objective measurements. Only a small proportion of the BMI values used in studies I (7%) and III (1%) were based on self-reported body weight or height. According to a reliability assessment conducted in the Health 2000 Survey, the agreement between self-reported and measured weight (ICC = 0.98) and height (ICC = 0.95) was high, indicating that the effect of self-reports on BMI classifications was slight. In Study III self-reported recalled weights and height were used. Currently obese persons tend to underestimate and currently low-weight persons overestimate their previous weights (Stevens et al. 1990; Perry et al. 1995; Tamakoshi et al. 2003). However, in this study, the effect of obesity on recall accuracy was controlled for, because information about current obesity was included in the categorization of obesity history. Apart from body weight, other factors that might affect the accuracy of recalled weights include gender, race and recall period (Stevens et al. 1990; Must et al. 1993; Perry et al. 1995; Tamakoshi et al. 2003). To reduce the potential bias, these variables, excluding race, were controlled for in our models. However, there is evidence that people can recall their past body weights over a long period of time with a good accuracy. For example, Tamakoshi and colleagues (2003) compared self-reported weight at age of 25 years with previously measured weight among Japanese men aged 34–61 years. They found a strong correlation between the recalled and measured weights ($r = 0.85$). Other studies have also shown high correlations ($r \geq 0.80$) between recalled and measured weight in young adulthood among middle-aged and older men and women (Stevens et al. 1990; Casey et al. 1991), justifying the use of recalled weights.

Analytical considerations

The cross-sectional designs in Studies I and II make it impossible to draw conclusions about the causality of the observed associations. However, with logistic regression analysis and sequential adjustment for medical conditions and biological indicators, it is possible to obtain important information on the associations between the studied variables. Furthermore, as this study was observational it can only provide preliminary evidence about the association and the mediating factors between obesity and walking limitation. Nevertheless, the results of this study can still be used as a basis for hypotheses to be tested in experimental studies, such as randomized controlled trials.

6.3 Future directions

Within the next few decades, the number of older obese persons is expected to increase rapidly in Finland and in other western countries for two concomitant reasons: the overall prevalence of obesity is rising and the number of older people living to very old age is increasing. Consequently, the number of persons with walking limitation caused by obesity or obesity-related conditions is likely to increase. Therefore, more studies are required on ways of preventing and alleviating obesity throughout the life-span, since avoiding excess weight gain is important in preventing functional limitation at older ages. More research is also needed on the effect of midlife weight loss and/or improvement in physical fitness on physical capacity in later life. Recent evidence suggests that moderate weight loss induced by combined dietary and physical exercise programs may improve mobility and physical functional capacity among older obese persons (Messier et al. 2004; Messier et al. 2005; Villareal et al. 2006). Further experimental research in collaboration with the behavioral sciences is, however, required to develop and evaluate feasible and effective interventions for older obese persons to prevent or decrease walking limitation.

In the present study, one of the aims was to recognize some of the factors that mediate the effect of obesity on walking limitation. Because these analyses were based on cross-sectional data, prospective studies and intervention trials are required to confirm the suggested pathways from obesity through diseases, low-grade inflammation, and decreased muscle strength to walking limitation. In the future, it would also be useful to examine other potential mediating factors, such as physical activity, lower limb strength, aerobic capacity, and joint flexibility in order to find factors that could be intervened to prevent walking limitation among obese persons. Studying the association of body fat mass and muscle mass, and especially fat infiltrated to muscle with sophisticated body composition measures might also provide new insights into the functional limitation of obese persons.

The association between obesity and walking limitation was examined in the present study from the epidemiological point of view, thus providing information about the phenomenon at the population level. However, at the individual level some obese persons are more prone to develop walking limitation than others. In addition to the factors covered in this study, more distant factors, such as genetic factors, may explain the large individual differences. Therefore, it would be interesting to use twin studies and quantitative genetic studies to examine whether there are genes that are associated with both obesity and walking limitation. Recognizing and targeting interventions at those persons who are genetically more vulnerable, and thus more prone to weight gain and functional limitation, might have a positive effect also at the level of public health.

7 MAIN FINDINGS AND CONCLUSIONS

The main findings and conclusions of the present study can be summarized as follows:

1. In persons aged 55 years or older, high BMI, large waist circumference, and high body fat percentage were associated with increased risk of walking limitation in a progressive manner. Obesity was more closely associated with walking limitation in older women than in older men.

2. Of the most common chronic conditions, knee osteoarthritis in women and type 2 diabetes in men were the strongest mediators in the association between obesity and walking limitation. In addition to diseases, low-grade inflammation and low muscle strength partially mediated the association between obesity and walking limitation.

3. High BMI and physical impairments measured at middle age predicted walking limitation 22 years later. In addition, longer duration of obesity increased the risk of walking limitation among persons aged 55 years or older.

4. Overweight or obese persons with coexisting diseases or physical impairments had a high risk of current or future walking limitation compared with the risk associated with excess body weight alone indicating that comorbidity and coimpairment have a negative effect on physical functioning.

In conclusion, the results of the present study indicate that obesity and obesity duration throughout the lifespan as well as obesity and coexisting conditions are important risk factors for older persons' walking limitation. The observations of the current study may be used as a basis when planning and targeting efficient interventions to prevent and alleviate walking limitation in older people. Future research using prospective and experimental settings is needed to confirm the role of diseases, low-grade inflammation, and decreased muscle strength on the pathway from obesity to walking limitation.

8 ACKNOWLEDGEMENTS

This study was carried out in the Department of Health and Functional Capacity at the National Public Health Institute in 2004–2007. The dissertation process has been a journey into the world of science. For me it was like the best journeys always are – lots of planning, searching for the right direction, moments of feeling completely lost and days of success, as well as illuminating discoveries and experiences. I have been privileged to share this educational journey with several wonderful persons and I would now like to express my sincere gratitude to them for their help and contribution to this study.

I am very much indebted to my supervisor, Professor Taina Rantanen, for her stimulating and skilful guidance. Taina's scientific dedication and her knowledge in the field of gerontological epidemiology are admirable. My special thanks go to Taina for her enthusiasm and encouragement throughout this work and for her valuable help in finding new directions for the future. I owe a large dept of gratitude to my other supervisor, Docent Seppo Koskinen for his scientific expertise and constructive comments to my queries. It has been a pleasure to work with such a warm personality. Seppo, thank you for being my supervisor, and sharing your knowledge and time with me. To my third supervisor, Docent Erkki Alanen, I am grateful for helping me with statistical issues and answering a novice's questions, especially at the beginning of this project.

I want to express my sincere gratitude to the official reviewers of this dissertation Professor Marjolein Visser and Docent Sirpa Hartikainen for their kind interest in and valuable comments on my work, and for revising it so promptly. Professor Kaisu Pitkälä is warmly acknowledged for agreeing to be my opponent in the public defense of this dissertation.

I am most grateful to Research Professor Arpo Aromaa, Head of the Department of Health and Functional Capacity, and Docent Antti Jula, Head of the Laboratory for Population Research, for the opportunity to work in this institute, for supporting me in this study, and making its outstanding research facilities available to me. I would like to thank very much the coauthors of the original articles, Ms. Päivi Sainio, Docent Markku Heliövaara, and Research Professor Antti Reunanen for their collaboration and valuable contribution to this study. Special thanks go to Päivi, for being a great fellow researcher and helping me to familiarize myself with the data of the Health 2000 Survey. I wish you the best of luck to your own research.

I warmly thank Professor Harri Suominen for leading inspiring doctoral seminars at the University of Jyväskylä as well as for being very helpful to me in my efforts to

manage the doctoral studies from a distance. I will always remember with a smile our conversations about sports outside of the research topics.

I express my sincere gratitude to the staff and participants in the Health 2000 Survey as well as those in the Mini-Finland Health Examination Survey. I am most grateful to have had the opportunity to use these unique databases gathered in Finland. In addition, I extend my thanks to all my colleagues in our department for your help and support during these years. Special thanks to Ms. Susanna Syrjäsuo for kind help in obtaining the literature and Ms. Riitta Nieminen for finalizing the layout of this thesis. Ms. Lea Heinonen-Eerola and Mr. Michael Freeman are greatly acknowledged for revising the English language of the original articles and the thesis.

This study was financially supported by personal grants from the Juho Vainio Säätiö and Finnish Cultural Foundation. They are both gratefully acknowledged.

I dare to say that the time spent outside the office have been vital for the progress of this work. In addition to my hope that my sport-related activities will prevent me from later life walking limitation, they have acted as a good counterbalance to the hours spent on the computer. To all my friends in the sport arenas and outside them, thank you for sharing your time and friendship with me.

Finally, I am most grateful to the people closest to me: to my parents Sisko and Kari for all their encouragement in anything that I have decided to do in my life, to my dear sister Siru for being there for me, and to my beloved husband Pekka for his endless support, constructive comments, and spurring me on throughout this project. Pekka, you mean the world to me.

Turku, June 2007

Sari

Sari Stenholm

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APPENDIX TABLE

APPENDIX 1

Appendix table. ***Summary of the studies examining the effect of obesity on mobility limitation in older adults***

Reference	Age at baseline (years)	n	Gender / country	Study design / inclusion criteria	Measures of obesity and mobility	Results
BMI						
Angleman et al. (2006)	55–74	1 918	M, F England	Prospective, follow-up 5 years No information about baseline mobility limitation	BMI: measured Mobility: measured walking speed (8 feet), self-reported difficulty in walking ¼ mile	BMI > 30 predicted ($p < 0.05$) walking difficulty in men and low walking speed and walking difficulty in women.
Bannerman et al. (2002)	70–103	1 272	M, F Australia	Prospective, follow-up 2 years The information about baseline mobility limitation was controlled in statistical analyses	BMI: measured Mobility: self-reported limitation in walking ½ mile and climbing stairs	The OR for mobility limitation in BMI > 30 was 2.14 (1.38–3.32).
Clark and Mungai (1997)	30–70	1 150	F USA	Cross-sectional	BMI: self-reported Mobility: self-reported difficulty in walking and climbing stairs.	BMI ≥ 30 was associated with mobility limitation ($p < 0.0001$). Prevalence of mobility limitation was 57% normal weight, 62% overweight, 76% obese, and 86% severely obese.
Coakley et al. (1998)	45–71	56 510	F USA	Cross-sectional	BMI: self-reported Mobility: self-reported limitation in walking and climbing stairs	BMI ≥ 30 was associated with mobility limitation ($p < 0.0001$). Physical functioning was 9% lower in obese and 15.5% lower in severely obese.
Davis et al. (1998)	55–93	705	F USA, Hawaii	Cross-sectional	BMI: measured Mobility: measured walking speed (6 m)	1 SD increase in BMI was associated with 5% reduction in walking speed ($p < 0.05$).
Davison et al. (2002)	≥ 70	2 917	M, F USA	Cross-sectional	BMI: measured Mobility: self-reported difficulty in walking ¼ mile, climbing stairs and agility	The ORs for mobility limitation were 2.26 (1.04–4.94) in severely obese men, and 1.55 (1.19–2.02) in overweight, 2.44 (1.63–3.67) in obese and 4.81 (2.33–9.91) in severely obese women.
Ebrahim et al. (2000)	40–59	5 717	M England	Prospective, follow-up 12–14 years No information about baseline mobility limitation	BMI: measured Mobility: self-reported difficulty in walking 400 yards, climbing stairs and agility	The OR for mobility limitation was 1.6 (1.0–2.5) in obese (BMI ≥ 28 kg/m^2) men.
He and Baker (2004)	51–61	7 867	M, F USA	Prospective, follow-up 4 years The information about baseline mobility limitation was controlled in statistical analyses	BMI: self-reported Mobility: self-reported difficulty in walking and climbing stairs	The RRs for mobility limitation were 1.27 (1.11–1.45) in overweight, 1.75 (1.55–1.96) in obese, and 2.43 (1.94–2.96) in severely obese.

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Appendix table continued

Reference	Age at baseline (years)	n	Gender / country	Study design / inclusion criteria	Measures of obesity and mobility	Results
Houston et al. (2005a)	45–64	9 416	M, F USA	Prospective, follow-up approx. 9 years No information about baseline mobility limitation (those were included who did not report diseases, poor self-rated health, or use of walking aids at baseline)	BMI: measured Mobility: self-reported difficulty in walking ¼ mile, climbing stairs and agility	High BMI predicted severe mobility limitation. Etc. an increase of 1 standard deviation of BMI increased the ORs for severe mobility limitation in 2.64 (2.37–2.94) in white women and 2.39 (2.01–2.84) in white men.
Houston et al. (2005b)	45–64	11 177	M, F USA	Retrospective, to the age of 25 years No information about baseline mobility limitation	BMI: current weight and height measured; recalled weight at the age of 25 Mobility: self-reported limitation in walking ¼ mile, climbing stairs, and agility	Obesity at age of 25 strongly predicted mobility limitation at ages 45–64 years in men and women ($p < 0.05$).
Jenkins (2004)	≥ 70	2 460	M, F USA	Prospective, follow-up 3 years The information about baseline mobility limitation was controlled in statistical analyses	BMI: self-reported Mobility: self-reported difficulty in walking several blocks and climbing stairs	The ORs for mobility limitation were 1.48 (1.08–2.03) in overweight and 2.07 (1.31–3.27) in obese persons.
LaCroix et al. (1993)	≥ 65	6 981	M, F USA	Prospective, follow-up 4 years Included only those who did not have mobility limitation at baseline	BMI: self-reported Mobility: self-reported difficulty in walking ½ mile and climbing stairs	The ORs for mobility limitation were 1.2 (1.0–1.4) in men and 1.3 (1.1–1.5) in women in > 80 percentile of BMI.
Larrieu et al. (2004)	65–101	8 966	M, F France	Cross-sectional	BMI: measured weight and self-reported height Mobility: self-reported difficulty in doing heavy housework, walking ½ mile and climbing stairs	The ORs for mobility limitation were 1.6 (1.2–2.1) for obese and 3.2 (1.6–6.3) for severely obese men, and 1.3 (1.1–1.6) for overweight, 1.6 (1.3–2.0) for obese, and 3.4 (2.2–5.3) for severely obese women.
Launer et al. (1994)	45–74	1 124	F USA	Prospective, follow-up on average 14 years Included only those who did not have mobility limitation at baseline	BMI: measured Mobility: self-reported difficulty in walking ¼ mile, climbing stairs and agility	The ORs for mobility limitation were 2.38 (1.44–3.39) for 45- to 59-year-old and 2.04 (1.20–3.49) for 60- to 74-year-old in the highest tertile of BMI.
Mendes de Leon et al. (2006)	≥ 65	4 195	M, F USA	Prospective, follow-up 3 + 3 years Included only those who did not have mobility limitation at baseline	BMI: measured Mobility: measured walking speed (8 feet), self-reported difficulty in walking ½ mile and climbing stairs	BMI ≥ 30 predicted mobility limitation ($p < 0.001$), but was not associated with change in mobility during follow-up.
Ramsay et al. (2006)	60–79	4 252	M England	Cross-sectional	BMI: measured Mobility: self-reported difficulty in walking ¼ mile and climbing stairs	The ORs for mobility limitation in two highest quintiles of BMI were 1.44 (1.08–1.92) and 1.99 (1.50–2.64) (p for trend < 0.001).

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Appendix table continued

Reference	Age at baseline (years)	n	Gender / country	Study design / inclusion criteria	Measures of obesity and mobility	Results
Waist circumference						
Angleman et al. (2006)	55–74	1 918	M, F England	Prospective, follow-up 5 years No information about baseline functional limitation.	WC: measured Mobility: measured walking speed (8 feet), self-reported difficulty in walking ¼ mile	The ORs for low walking speed in the highest quartile of WC was 2.4 (1.4–4.1) in men and 3.0 (1.9–4.8) in women.
Bannerman et al. (2002)	70–103	1 272	M, F Australia	Prospective, follow-up 2 years The information about baseline mobility limitation was controlled in statistical analyses	WC: measured Mobility: self-reported limitation in walking ½ mile and climbing stairs	The OR for mobility limitation in WC > 1.02 m in men and 0.88 m in women was 1.43 (0.99–2.08).
Guallar-Castillón et al. (2007)	≥ 60	1 129	M, F Spain	Prospective, follow-up 2 years Included only those who did not have mobility limitation at baseline	WC: measured Mobility: self-reported limitation in walking 200–300 m and climbing stairs	The ORs for mobility limitation in the highest quintile of WC was 2.17 (1.15–4.09) in men (> 1.11m) and 1.81 (1.02–3.20) in women (> 1.07m).
Houston et al. (2005a)	45–64	9 416	M, F USA	Prospective, follow-up approx. 9 years No information about baseline mobility limitation (included those who did not report diseases, poor self-rated health, or use of walking aids at baseline)	WC: measured Mobility: self-reported difficulty in walking ¼ mile, climbing stairs and agility	High WC predicted severe mobility limitation. Etc. an increase of 1 standard deviation of WC increased the ORs for severe mobility limitation in 2.66 (2.39–2.96) in white women and 2.74 (2.28–3.29) in white men.
Ramsay et al. (2006)	60–79	4 252	M England	Cross-sectional	WC: measured Mobility: self-reported difficulty in walking ¼ mile and climbing stairs	The ORs for mobility limitation in two highest quintiles of WC were 1.35 (1.00–1.82) and 1.95 (1.47–2.59) (p for trend < 0.001).
Visser et al. (1998a)	72–95	753	M, F USA	Cross-sectional	WC: measured Mobility: self-reported difficulty in walking ½ mile and agility	High waist circumference was not associated with mobility limitation.
Body fat mass						
Broadwin et al. (2001)	55–92	1 051	M, F USA	Cross-sectional Prospective, follow-up 4 years Included only those who did not have mobility limitation at baseline	Fat percentage: BIA Mobility: self-reported difficulty in walking 2–3 blocks and climbing stairs	The ORs for incident mobility limitation were 3.9 (1.5–10.0) in men and 3.6 (1.8–7.4) in women. No cross-sectional association was found between high fat percentage and mobility limitation.
Lebrun et al. (2006)	56–73	396	F Netherlands	Cross-sectional	Fat mass: DXA Mobility: measured walking speed (8 feet), standing balance, and chair rising	Higher fat mass was associated with lower physical performance (p < 0.0001). A 10 kg increase in fat mass was associated with 0.5 point lower physical performance.

Continued overleaf

Appendix table continued

Reference	Age at baseline (years)	n	Gender / country	Study design / inclusion criteria	Measures of obesity and mobility	Results
Ramsay et al. (2006)	60–79	4 252	M England	Cross-sectional	Fat mass: BIA, fat mass index = fat mass / $(\text{height})^2$ Mobility: self-reported difficulty in walking ¼ mile and climbing stairs	The ORs for mobility limitation in the highest quintile of fat mass index was 1.59 (1.20–2.12) (p for trend < 0.0001).
Sternfeld et al. (2002)	55–96	1 655	M, F USA	Cross-sectional	Fat mass: BIA Mobility: measured walking speed (feet/second during 60 s test) and self-reported difficulty in walking, climbing stairs and agility	The ORs for mobility limitation with absolute increase in fat mass (kg) were 1.09 (1.05–1.12) in men and 1.08 (1.06–1.10) in women.
Visser et al. (1998a)	72–95	753	M, F USA	Cross-sectional	Percent body fat: DXA Mobility: self-reported difficulty in walking ½ mile and agility	The ORs for mobility limitation were 3.04 (1.09–8.50) in the highest tertile of body fat percentage in men. In women, the ORs the middle and highest tertile of body fat percentage were 2.17 (1.07–4.37) and 4.07 (2.00–8.28).
Visser et al. (1998b)	65–100	4 809 3 274	M, F USA	Cross-sectional Prospective, follow-up 3 years Included only those who did not have mobility limitation at baseline	Fat mass: BIA Mobility: self-reported difficulty in walking ½ mile and climbing stairs	Three highest quintiles of body fat mass were associated with mobility limitation 1.33 (1.02–1.74), 1.38 (1.05–1.80), and 2.94 (2.27–3.82). Two highest quintiles of body fat predicted incident mobility limitation 1.67 (1.22–2.31) and 2.22 (1.58–3.10).
Visser et al. (2002)	70–79	2 979	M, F USA	Cross-sectional	Muscle fat infiltration: CT Mobility: measured walking speed (6 m) and chair rising	The greater fat infiltration into the muscle was associated with poorer lower extremity performance in men and women ($p < 0.05$).
Visser et al. (2005)	70–79	3 075	M, F USA	Prospective, follow-up 2.5 years Included only those who did not have mobility limitation at baseline	Muscle fat infiltration: CT Mobility: self-reported difficulty in walking ¼ mile and climbing stairs	The HRs for mobility limitation in the lowest quartile of muscle tissue attenuation was 1.92 (1.31–2.83) in men and in the two highest quartiles 1.68 (1.20–2.35) and 1.68 (1.22–2.33) in women.

Notes: Results are from adjusted model if not otherwise stated. Values in parenthesis indicate 95% confidence interval for odds ratios (OR), risk ratios (RR) and hazard ratios (HR). M = male; F = female; BMI = body mass index; WC = waist circumference; BIA = bioelectric impedance analysis; CT = computed tomography; DXA = dual energy x-ray absorptiometry. BMI 25–29.9 kg/m^2 refers to overweight, 30–34.9 kg/m^2 to obesity, and ≥ 35 kg/m^2 to severe obesity.