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NUTRITIONAL STATUS AND COGNITIVE FUNCTION IN FRAIL ELDERLY SUBJECTS

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Stockholm 2004

ABSTRACT

Longevity, frailty and chronic disease are often associated with protein energy-malnutrition (PEM). Subjects with dementia are at particular risk for PEM. The overall aims of this thesis were to evaluate relationships between nutrition, cognition and functional capacity and to assess interventional means of developing the nutritional care of elderly.

In study I and II, the nutritional status and the cognitive function were examined in 28 and 80 service flat (SF) residents. Furthermore, the effect of a nutrition education programme to SF care staff was evaluated. In study III, 22 and 14 subjects living in two group living units for demented (GLD) participated and the effects of nutritional supplementation and education to care personnel were evaluated. In study IV, possible relationships between weight, weight change and cognitive function were studied in 231 patients, admitted to a geriatric ward for examination of cognitive dysfunction. Seven-year mortality in relation to dementia diagnosis and nutritional status was also studied (IV).

The nutritional status was assessed by Body mass index (BMI=kg/m^2), triceps skin fold (TSF), and arm muscle circumference (AMC). Study I and II included a modified Subjective Global Assessment (SGA). Muscle strength was measured with a Harpenden Grip Strength Dynamo-Meter® (I, II). As biochemical nutritional markers in serum, albumin, transferrin, haemoglobin, C-reactive protein (CRP), vitamin B12, folic acid and insulin-like growth factor-1 (IGF-1) (I-III) were analysed. Cognitive and functional status was assessed by the Mini Mental State Examination (MMSE) (0-30p, I-IV), Clinical Dementia Rating Scale (CDR) (0-3, III) and Katz′ADL-index (I-III). Care personnel at the SF (I-III) complexes attended 12-hour nutritional education programmes. The care personnel answered a questionnaire before and after the education that reflected their knowledge and attitudes about nutrition in elderly (I, II). Oral supplements (410 kcal/1720 kJ) were given daily during 5 months to residents in one of the two GLD units and the personnel attended a nutritional education programme (III). Mortality data (IV) were obtained from Swedish population records.

Up to one third of the SF residents were assessed as malnourished or at risk for PEM according to SGA (I-II). The education program tended to improve the knowledge of the care personnel in study I. In study II there was no significant difference in improvement between the staff at the two SF complexes. Objective measures of nutritional status and cognitive function in the residents was not changed at 5- and 6-months follow-ups, whereas SGA appeared to improve after the educational intervention (II). The combined intervention in study III resulted in a weight gain of 3.4 ±11.2 kg (p=0.001) 6 months later, that was not seen in the control group. The weight gain was not related to an improvement in ADL-capacity or cognitive function (MMSE). A BMI <23 was noticed in more than half of 231 patients admitted for diagnostic evaluation of cognitive function (IV). The weight increased by 0.5 kg (p<0.001) during a 3-week hospital stay. Concurrently, an increase in MMSE by 1 point was noticed (p=0.0001). The changes in weight and MMSE did not correlate. BMI <23 seemed to predict shorter survival (OR 3, 95% CI 1.3-6.7), even after adjustment for age, gender and co-morbidity, whereas type and degree of dementia were not related to 7-year mortality.

In conclusion, a limited nutrition education programme to care personnel did not affect the nutritional status of SF residents 5-6 months later. No overt improvements in the knowledge of the care staff were observed. Nutritional status was related to cognitive function. Care staff education and oral supplementation resulted in weight gain in GLD residents. A BMI <23 seemed to predict mortality in individuals with cognitive failure. More studies are needed to settle the relationships between nutrition and cognition in elderly individuals.

LIST OF PUBLICATIONS

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

I. Faxén-Irving G, Andrén-Olsson B, Cederholm T. Nutritional and cognitive status in elderly subjects living in service flats, and the effect of nutrition education on personnel. Gerontology 1999;45:187-194.

II. Faxén-Irving G, Andrén-Olsson B, Geijerstam A, Basun H, Cederholm T. Nutrition education for care staff and possible effects on nutritional status in residents of sheltered accomodation – a controlled study. Submitted.

III. Faxén-Irving G, Andrén-Olsson B, Geijerstam A, Basun H, Cederholm T. The effect of nutritional intervention in elderly subjects residing in group-living for the demented. Eur J Clin Nutr 2002;56:221-227.

IV. Faxén-Irving G, Basun H, Cederholm T. Nutritional and cognitive relationships and long-term mortality in patients with various dementia disorders. Submitted.

LIST OF CONTENTS

LIST OF ABBREVIATIONS

AD	Alzheimer's disease
ADL	Activities of daily living
AMC	Arm muscle circumference
BMI	Body mass index
CI	Confidence interval
CDR	Clinical Dementia Rating (scale)
CRP	C-reactive protein
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (revised fourth edition)
FFQ	Food-frequency questionnaire
GLD	Group-living for the demented
Hcy	Homocystein
HGS	Hand-grip strength
IGF-I	Insulin-like growth factor I
MCI	Mild cognitive impairment
MMSE	Mini mental state examination
MNA	Mini nutritional assessment
ONS	Oral nutritional supplements
OR	Odds ratio
RCT	Randomised controlled study
PEM	Protein energy malnutrition
SD	Standard deviation
SF	Service flat
SGA	Subjective global assessment
TSF	Triceps skinfold thickness
VaD	Vascular dementia

INTRODUCTION

DEMOGRAPHIC TRENDS IN SWEDEN

The average age of the population in developed countries is increasing due to falling birth rates and increasing longevity. Currently, approximately 17% of the Swedish population is >65 years old with the elderly above 85 as the most rapidly growing group. The average life expectancy in Sweden in 2003 was 82.5 years for women and 78 years for men. The difference in life expectancy between men and women has decreased from around 6 to 4.5 years since 1980 (1).

Recently, results from a nationwide investigation of health and functional capacity in 561 elderly in Sweden, the SWEOLD study, somewhat unexpectedly showed that health and functional capacity has deteriorated in the very advanced ages, i.e. 77-98, between 1992 and 2002 (2). The disability was more pronounced in women than in men. This was also found in another study from the Kungsholmen Project (3). The SWEOLD study reflects the development in health care needs of the elderly since the ÄDEL-reform was introduced in 2002. This reform resulted in a reduction of 60 % of hospital beds and gave the municipalities the entire responsibility for long term care of the elderly (4).

SHELTERED HOUSING

In 2003, approximately 111,000 elderly, i.e. 7% of the Swedish population, lived in sheltered housing, while 128,000 received home help support (5). Sheltered housing includes service flats, old people's homes, group living for the demented, nursing homes and day care facilities.

Service flats (SF) are a type of accommodation where the residents live in their own needs-adapted flats, located in SF complexes. The residents usually have access to a restaurant in the SF complex where they can eat lunch. District nurses give medical care and the residents have access to care staff if needed. SF complexes were introduced in Sweden in the late 1960s and large-scale production started in the mid-1970s. They were primarily intended for healthy elderly people who could continue living there when they became frail and in need of support. Currently mainly frail and chronically ill people move in to SFs. This is most likely due to the increasing demands on community care over recent decades.

Group-living for demented elderly people (GLD) is a form of care that emerged in Sweden during the latter half of the 1980s. This form of intermediate care provides a home-like environment where demented residents live in their own flats with common areas for meals and social activities. The caregivers are usually specially trained for the care of people with dementia. Less anxiety, better orientation capacity and more opportunities to take part in daily activities, such as cooking, are some of the advantages of GLD as compared to living in traditional institutions (6-7).

2004-08-30

ERRATA

Nutritional status and cognitive function in frail elderly subjects
Gerd Faxén Irving

Introduction: Page 6, 2nd paragraph, line14: 2002 should be 1992.
Results: Page 27, 4th paragraph, line 9: (28%) should be (25%).
Paper 3. Page 225, 1st paragraph, line 4. After appeared "*to deteriorate*"should be added.

NUTRITION

PREVALENCE AND CAUSES OF MALNUTRITION IN THE ELDERLY

Malnutrition literally means bad or faulty nutrition. As there is no universally accepted definition, the following is suggested: Malnutrition is a state of nutrition in which a deficiency, excess or imbalance of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form and function, and clinical outcome (8). Different types of malnutrition are defined in the literature; Marasmus is caused by deficient energy intake, characterised by wasting of fat depots and of skeletal muscle, whereas kwashiorkor is caused by extensive loss of visceral proteins while fat stores are maintained (9). Chronically ill elderly people usually have a mixture of marasmus and kwashiorkor, i.e. protein-energy malnutrition (PEM) (10). PEM or risk of PEM is common in the elderly, occuring in 25-60% of elderly subjects admitted to hospital (11-18). The occurrence varies between 1-7% in free living elderly (19-21). In sheltered accommodation, an average of one-third are assessed as being malnourished (22).

Poor dentition and bad oral health decreases the ability to eat and leads to insufficient food intake (23-25). Pro-inflammatory cytokine activity relates to cachexia in chronic disorders and may be a dominant factor causing anorexia that leads to PEM (26-28). Older patients are more likely than younger ones to lose their appetites in response to physiological stress (29). Dysphagia, present in approximately 25% to 32% patients with stroke, is another risk factor for PEM (30). Up to 16% of stroke patients may be malnourished on admission to hospital and this tends to worsen during the hospital stay, especially in the more dependent (31-32). Cognitive decline is associated with malnutrition. Finally, loneliness and social isolation can lead to decreased intake and

depression, which can then result in more nutritional deficiencies (33-34).

CONSEQUENCES OF MALNUTRITION

Malnutrition causes fatigue, apathy and depression (35). Loss of muscle mass and muscle strength is now denoted sarcopenia (36-37). Involuntary weight loss combined with functional decline may be called "failure to thrive" in the elderly (38). The immune system is weakened with impaired immune responses (39-40). Several investigators have shown increased short- and long-term mortality in malnourished older people (41-46). Moreover, malnutrition increases respiratory and cardiac complications, infections, pressure-ulcers and delayed ulcer healing (47-52). Undernutrition is also associated with falls (53) and fractures (54). Community-dwelling older people at risk for malnutrition were recently shown to be at increased risk of frequent and prolonged hospitalisation and falls (55).

In November 2003, the Council of Europe, Committee of Ministers adopted a resolution on food and nutritional care in hospitals to "raise the levels of health protection of consumers in its widest sense". The council has considered that undernutrition among hospital patients leads to extended hospital stays, prolonged rehabilitation, diminished quality of life and unnecessary health care costs and that there is an unacceptable number of undernourished hospital patients in Europe. This document includes recommendations about nutritional assessment and treatment in hospitals (56).

NUTRITIONAL ASSESSMENT

In 1991, Mowe, et al stated that malnutrition was undiagnosed in 60% of patients admitted to hospital (57). In the majority of patients that are undernourished at hospital admittance, undernutrition develops further while in hospital (14). Today there are several screening tools for detecting under-

nutrition, or risk for undernutrition. Most of them include such information as current weight, height, BMI, weight loss, recent food intake and/or existing eating difficulties. Loss of appetite may be an early indicator of anorexia of ageing leading to malnutrition in the frail elderly (29,58) and a questionnaire for assessing appetite in the elderly has been proposed (59).

The European Society for Clinical Nutrition and Metabolism (ESPEN) developed guidelines for nutrition screening in 2002 (60). The guidelines recommend the following screening tools: The malnutrition universal screening tool (MUST) (61) for both the community and hospitals; Nutritional risk screening NRS-2002 (62), for use in hospital settings; Mini Nutritional Assessment (MNA) for the elderly. Guidelines for nutritional care in both community and hospital settings have recently been published in Sweden (2004).

Anthropometry

The body mass index (BMI), kg/m^2 is currently the most utilised weight and height index. In elderly subjects, factors like osteoporosis, fluid balance and ability to participate in the examination can influence the measurement. Arm span (63-65), knee height (14,66) or measuring length of forearm (ulna) (67) can be used to predict height. The BMI cut-off values, 20-25 for adults, have been discussed and different cut off values for elderly individuals have been proposed. Potter, et al suggested a BMI <23.5 to define underweight in community and hospital settings (68), Beck & Ovesen, based on a review of the literature, suggested a range of 24-29 kg/m^2 for hospitalised elderly patients (69). Low BMI values also predicts mortality in the elderly (41-42). BMI needs to be combined with other markers to diagnose malnutrition (63).

To estimate body fat and subcutaneous fat mass, measurements of skin fold thickness can be made over the triceps muscle, i.e. triceps skinfold (TSF) on the mid-posterior facet of the upper arm. From the recordings of TSF and mid-upper arm circum-ference (AO), the arm muscle circumference (AMC) can be calculated according to the formula AMC (cm) = AO (cm) – π x TSF (cm) (70).

Muscle strength measurements

Hand-grip strength (HGS) is a measure of strength of the hand and the fore-arm muscles and is measured in kilograms using a handgrip dynamometer (71-72). HGS is an easily accomplished measurement of muscle function and is positively associated with nutritional status (73-75). It may also predict postoperative complications (76). A low HGS is associated with serious postoperative morbidity (77). Although HGS is a quick, easy and reproducible test, it has to be combined with other tests of nutritional status (78).

Biochemical indices

Serum albumin, transferrin and insulin-like growth factor I (IGF-I) are commonly used as indicators of nutritional status. Caution must be taken in interpreting results of serum protein measurements since they are influenced by many factors. Both albumin and IGF- I are negative acute-phase reactants, meaning that serum con-centrations can drop precipitously in response to sepsis, major surgery and other forms of acute severe physiological stress (79) as a result of increased vascular permeability. Therefore, those markers seem more closely linked to co-morbidity and inflammation than to nutritional status (80). C-reactive protein (CRP), a commonly used marker of inflammation, correlates inversely to albumin.

In outcome studies conducted within hospitals and long-term care institutions, albumin has been found to be an important prognostic indicator of morbidity and mortality (81-83). As part of other nutritional data, serum protein measure-ments provide valuable information

regarding nutritional status, prognosis and treatment.

Plasma IGF-I levels in elderly patients are influenced by age-related decline in growth hormone secretion and by many other factors (84-85). IGF-I is a non-specific but sensitive indicator of changing health status (86) and adequacy of nutrient intake. Low IGF-I predicts serious complications and death among hospitalised elderly patients (87).

Subjective global assessment

The Subjective Global Assessment (SGA) is a method initially developed to predict nutrition-related complications in patients undergoing surgery (88). SGA has been adjusted for Swedish conditions (89) and has been used to assess nutritional status in geriatric patients (90-91). SGA includes questions regarding ongoing weight loss, changes in dietary intake, gastrointestinal symptoms and functional capacity. This is combined with a physical examination of subcutaneous fat and muscle wasting, sacral and ankle oedema or ascites. The patient is categorised by the examiner as: well nourished, at risk of being malnourished or severely malnourished.

Mini nutritional assessment

MNA was developed for geriatric patients. It is an 18-item questionnaire (0-30 points), that includes risk factors relevant to the elderly.

MNA includes anthropometric measurements (BMI, MAC and calf circumference (CC)), reports of recent weight change, pharmaceutical consumption, acute diseases, neuropsychological problems and mobility. Pressure sores/skin ulcers are registered and six questions about dietary intake are posed. Finally the subjects are asked to make a self-assessment of their perceived nutritional and health status (92). A total score of less than 17 points indicates malnutrition, 17-23.5 points indicates risk of malnutrition, and ≥24 points indicates well nourished.

EFFECTS OF NUTRITIONAL INTERVENTION IN ELDERLY SUBJECTS

Oral supplement in multiple non-malignant disorders

Nutrition treatment studies in chronically ill patients have several methodological problems: there is no generally accepted definition for PEM, a wide range of outcome variables are used and patient compliance with supplementation is uncertain.

Recently, Akner & Cederholm published a systematic review of 26 nutritional intervention studies in geriatric patients published up to year 2000 (35). In almost all studies, oral nutritional supplements (ONS) were used as interventions. The intervention period was from 2 weeks to 6 months and included between 12-435 patients. Twenty of the studies, of which 11 were randomised controlled trials (RCT), noted an improvement in anthropometric or biochemical measures in the intervention groups. Ten (6 RCT) also found an improvement in functional status. One RCT described how the oral supplement reduced the number of fall-related traumas. Most treatment studies lack information on total energy intake, and patients' ability to follow prescription of ONS varies. Some studies indicate that ONS can reduce food intake, but most studies note an increase in intake without loss of appetite. The authors conclude that the available treatment data indicate that nutritional supplements, either alone as balanced or protein-rich liquid nutrient drinks or in combination with hormonal administration, can have positive effects when given to chronically ill, non-malignant patients with manifest PEM or at risk of PEM. They ask for randomised controlled long-term studies of the effects of defined nutritional programs in chronically ill and frail elderly with a focus on determining clinically relevant outcomes.

Similar data are presented in a 2002 Cochrane meta analysis, of protein and energy supplements (93) that includes RCT and quasi-randomised controlled trials of oral protein and energy supplementation, indexed in MEDLINE from 1966 to March 2001. Patientgroups in critical care and recovering from cancer were excluded. Thirty-one trials with 2,464 randomised participants are included in the review, which concludes that supplementation appears to produce a small but consistent weight gain. There was a statistically significant beneficial effect on mortality and a shorter length of hospital stay. Additional data from large-scale multi-centre trials are needed to provide clearer evidence of benefits from protein and energy supplements on mortality and length of hospital stay.

Stratton, et al reviewed the effects of ONS in elderly hospital patients involving 12 RCT and 5 non-randomised trials between 1978-2001 with durations of 3-26 weeks. They also reviewed the elderly in community settings, in 10 RCTs, with ONS providing 200-600 kcal over 4-24 weeks, 1985-2000 and 7 non-randomised trials in elderly receiving ONS at home, 1985-1998 (8). Key findings in hospital trials were that ONS can improve intake of energy, protein and micronutrients without substantially reducing food intake that may lead to weight gain or attenuate weight loss. Mortality is significantly reduced and hospital stays may be reduced. Key findings of ONS in community patients were that ONS can increase total energy and nutrient intake and may improve body weight and muscle mass. The ONS plays an important role in preventing nutritional status deterioration. In malnourished elderly subjects it may be too late to expect to see effects in function, quality of life and survival (94-95). In a study of nursing home residents by Larsson, et al the effect of ONS on mortality was most evident in the non- malnourished subjects (96).

New treatment approaches

When given in combination with megastrol acetate, often used in cancer-related wasting, ONS showed promising results (97). Fiatarone, et al found positive effects when supplements and resistance training were given simultaneously. Supplementation given alone did not improve muscle strength or physical function (98). A model of distribution of oral sip-feeds (3 x 120ml =540 kcal) that was recorded in the medicine prescription chart was recently tested (99). Consumption was monitored by nurses, and non-compliance was noted using standard codes used for other medicines, which identify reasons for non-compliance. Energy intake was improved by the prescription of small quantities of oral sip-feeds delivered during medication rounds. The method secures nursing compliance with nutritional support and is accompanied by a high level of patient compliance.

Strategies to increase intake of ordinary food

Fortification of food by increasing the energy density content can increase energy intakes and body weight (100-102). Environmental changes may be beneficial in improving nutritional intake. There is some evidences that consumption of small amounts of alcohol with meals may stimulate food intake (103). Food taste and smell intensification may also be beneficial (104-105). Eating in a group can encourage oral intake and providing a communal setting for older at-risk individuals may be beneficial (106). A combination of various techniques to increase food intake may be advised.

DEMENTIA

PREVALENCE AND DIAGNOSES

Dementia disorders are age-related (107), and since the number of old people is steadily increasing, more people will develop dementia. Approximately 8% of older people between the ages of 75 and 85 are assumed to suffer from dementia (108). By the year 2020, the WHO predicts there will be nearly 29 million demented people worldwide (109). The disease affects not only the patients but also their relatives, many of whom are involved in informal care.

Dementia is commonly recognized through use of codified criteria, such as the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, 1994 (DSM-IV) (110). Here dementia is defined as a clinical syndrome characterised by the development of multiple cognitive deficits that are severe enough to interfere with daily functioning, including social and professional functioning. The cognitive deficits should include memory impairment and at least one of other cognitive domains, such as aphasia, apraxia (difficulties in performing ordinary tasks), agnosia or disturbance in executive functioning.

Alzheimer's disease (AD) is the most common type of dementia and accounts for more than 50% of all dementia cases. Vascular dementia (VaD) is diagnosed in about 15-20% of the patients (111). Mixed dementia is diagnosed in patients with changes that are typical in both AD and VaD (112). Mild cognitive impairment (MCI) is currently, the most widely used term to indicate non- demented elderly people with a mild memory or cognitive impairment that cannot be accounted for by any recognised medical or psychiatric condition (113). MCI may be a preclinical phase of dementia, with estimates of 12% of MCI patients developing dementia in 1 year (114) and, 20% over 3 years (115). Identification of possible risk factors for

conversion of MCI to dementia may be crucial for prevention. Fronto-temporal dementia (FLD), characterised by behavioural and emotional disturbances, is less frequent and is diagnosed in less than 10 % of all cases. The aetiology is unknown.

In the 1990´s, pharmacological treatment was introduced with symptomatic effects on cognition, behaviour and function. The drugs most experienced so far are acetylcholinesterase inhibitors (AChEIs) which act by increasing acetylcholine in the brain (116). The cholinergic system is strongly related to cognitive functions, especially to memory functions. There is no drug that can prevent or stop the development of the disease, but worldwide research is underway. Providing adequate nutrition might be a determinant in good survival in institutionalised and frail demented subjects.

Reports from Alzheimer's Awareness Week in the UK, July 2000, highlighted the fact that many caregivers and people with dementia themselves have been told by health professionals that weight loss is part of the illness, and that little or nothing could be done about it. However, many recent studies have used weight gain as an outcome variable and have provided evidence that it is possible to prevent or reverse weight loss in people with dementia (117).

NUTRITIONAL IMPLICATIONS IN ALZHEIMER'S DISEASE

To find a way to improve the quality of life for the elderly, it is important to understand the relationships between nutrition and cognition (118).

Adverse associations?

Midlife vascular risk factors such as type 2 diabetes, hypertension, dietary fat intake, high cholesterol and obesity have emerged as important influences on the risk of both vascular dementia and AD (119-120). Epidemiological studies have reported that

high intakes of total fat, saturated fat, total cholesterol, caloric intake and overweight increase the risk for incident dementia and AD (119,121-125). Consequently, nutrients that are identified as risk factors for cardiovascular disease may also be negative for the brain and cognitive functions.

The association between aluminium and AD remains a controversial subject with no strong evidence for a linkage to AD (126-128).

Beneficial associations?

Omega-3 fatty acids
The role of dietary fat in dementia has attracted increasing interest. Fatty acids could be involved in cognition through several mechanisms. In addition to providing vascular protection, the n-3 fatty acids could reduce inflammation in the brain and may have a specific role in brain development and regeneration of nerve cells. Cognitive function was inversely related to a high fish consumption in the Zutphen Elderly Study (129). Results from the Rotterdam Study, a single-centre prospective population-based study of 5000 non demented people >55 years (122) showed that high intakes of total fat, saturated fat and cholesterol were associated with an increased risk of dementia whereas an inverse association between fish consumption and AD was found. The follow-up period was 2 years. New results from this study with a follow-up period of 6 years were recently presented (121). The data from the first study was not repeated in this study, making the evidence unclear. Another Dutch study was performed in 1,600 younger people aged >45 with cognitive tests at start and at follow-up 6 years later. Consumption of fish and intake of eicosa-pentaenoic acid (EPA) and docosa-hexaenoic acid (DHA) was inversely related to risk for impaired cognition. This remained after correction for age, gender, education, smoking, alcohol and energy intake (130). A French cohort study of 1600 individuals aged >68 with a seven year follow-up, found that elderly people who eat fish or seafood at least once a week are at lower risk of developing dementia, including AD (131). Finally, a study from Chicago included 815 people aged >65, at risk for dementia where 130 individuals developed AD in 3 years. It was concluded that fish consumption once a week or more reduced the risk of developing AD by 60% (132). Most of the studies presented in this field are epidemiological and usually the food-frequency questionnaire method is used to collect data on food intake. Experimental studies in this field are needed.

Antioxidants
Oxidative processes have been suggested as contributing factors in the development of AD, and therefore antioxidants might have a protective and preventive effect. Whether dietary intake of vitamin E and other antioxidant nutrients prevents oxidative stress is controversial. Prospective and longitudinal studies show inconclusive results.

Morris, et al found that vitamin E from food, but no other antioxidants, was associated with a reduced risk of developing AD in 815 individuals aged ≥65, followed up for a mean of nearly 4 years. Data were adjusted for age, education, sex, race, APOEe-4, and length of follow-up (133). In the Rotterdam study, 5,395 individuals were followed for a mean of 6 years. A reduced risk of AD was associated with intake of vitamin E and vitamin C, (134). A RCT with high doses of vitamin E (2,000 IU/d) in patients with moderate to severe Alzheimer's disease resulted in a longer time before institutionalisation and a delayed time to deterioration of ADL, although cognitive function did not improve (135). The Nurses Health Study found that long-term, current users of vitamin E with vitamin C had significantly better mean performance than did women who had never used

vitamin E or C or used vitamin C alone (P=0.03) (136). In the Honolulu-Asia Aging Study of 2,459 Japanese-American, 45-68 year old men, no associations were found between intakes of beta-carotene, flavonoids, and vitamins E and C with the risk of dementia or its subtypes (137). Finally, the MRC/BHF Heart Protection Study, including 2,053 adults, aged 40-80 with coronary heart disease, found no treatment differences between those allocated to antioxidant vitamin supplementation or placebo, in individuals defined as cognitively impaired or in mean cognitive scores after 5 years of treatment (138).

Most work has focused on supplementation with vitamin E, for which the primary variant is α-tocopherol, but dietary vitamin E is primarily γ-tocopherol. Some authors have suggested that γ-tocopherol may have stronger antioxidant properties than does α-tocopherol. No large-scale human studies to date have specifically addressed the influence of tocopherol variants on cognitive outcomes. Although findings are inconsistent, the number of studies that argue for a protective effect of antioxidants on cognitive function are increasing (139).

Alcohol - wine
The preventive effect from low doses of alcohol through its antioxidant and cardiovascular mechanisms has also been discussed. A possible mechanism for the protective effect of wine is the properties of polyphenoles, which are most prominent in red wine. Some studies have found a lower risk among wine consumers (140-142) compared to other alcohol consumers. Others did not find such a difference according to the type of alcohol consumed, suggesting a protective effect of alcohol itself on vascular factors (143). In a study of 2,950 initially non-demented subjects, the PAQUID-study found that moderate drinkers had a decreased relative risk of developing dementia (RR=0.56) compared to non-drinkers (144).

B 12, folic acid and cognition
B 12 deficiency is common in the older population with a prevalence of 13% (145). Low B 12 levels in the healthy elderly and in demented subjects are often associated with cobalamin malabsorption, where atrophic gastritis has been reported to be the main cause of B 12 deficiency (146-147). In a Swedish population sample, the prevalence of various gastritis ranged from 28% at ages 35-44 to 81% at ages over 75 (148-149). Atrophic gastritis accounted for 55% of the cases (150).

Current studies suggest that low levels of vitamin B12 as well as folic acid may be part of the aetiology in AD. A functional deficit of vitamin B12 and folic acid may be present although serum levels are within reference limit. The amino acid homocysteine (Hcy) is a sensitive but non-specific marker of vitamin B 12 and folic acid deficiency. The association between Hcy and cognitive function is much stronger than that of B 12/ folic acid and cognition. Many studies have found an association between vitamin B12/ folic acid deficiency and/or elevated Hcy levels and cognitive impairment (151-152). Clarke, et al, in a case-control study of 164 patients with a clinical diagnosis of AD, found that patients with elevated Hcy, >11.1μmol/l showed a more rapid progression of AD over 3 years than did those with Hcy below this value (153). Wang, et al reported that of 370 cognitively intact people aged ≥70, those with initial low B12/ folic acid levels were at greater risk of developing AD (154). No relationships between markers for gastritis and hyper-Hcy, dementia disorders and B12/folic acid deficiency were found in a study by Nägga et al (155). Some treatment studies have reported improvement of cognition with vitamin B12 and folic acid. The best effects have been achieved in patients with short duration of the disease and mild to moderate cognitive impairment. A Swedish study on patients with mild to moderate

cognitive impairment and elevated Hcy levels found an improvement in 14 out of 17 patients with a daily treatment combination of B 12 and folic acid for 2 months (156). A Cochrane analysis in 2002 concluded that there is insufficient evidence of any effect of vitamin B12 therapy on cognitive function in older people with low serum vitamin B12 levels and dementia (157). Clinical trials are needed to evaluate the role of Hcy in cognitive decline and the effect of Hcy-lowering vitamins in those elderly who have developed mild cognitive impairment.

Gingko Biloba
Gingko Biloba, extracts of the leaves of the maidenhair tree, has been used in China as a traditional medicine for various health disorders, for at least 5,000 years. The mechanisms are thought to reflect the action of several components of the extract, i.e. flavonoids, terpenoids and terpene lactones. The effects described are: increasing blood supply by dilating blood vessels, reducing blood viscosity, modifying neurotransmitter systems and reducing the density of oxygen free radicals (158). In 1992 a review was published in The Lancet showing a beneficial effect of Ginkgo for patients with cerebral insufficiency in 29 of 40 RCT:s (159). Yet the methodological quality of many of the trials was poor and covered many different health problems. Later, several rather well designed trials, focused on dementia, have also shown positive effects of Ginkgo (160). Along with improved study methodology, there has been a tendency for smaller effects to be reported. In a 1999 systematic review, of the clinical evidence of Ginkgo as a symptomatic treatment for dementia, it was concluded that Ginkgo was more effective for dementia than a placebo (161). Some recent double-blind RCT studies show conflicting results (162-163). Cochrane's analysis (2002) concludes that Gingko Biloba appears to be safe to use, with no excess side effects, compared with a placebo, that many of the early trials used unsatisfactory methods, were small and publication bias could not be excluded (158).

Concluding remarks

A diet that is healthy and considered to prevent cardiovascular disease may also protect against age-related cognitive decline. Results from epidemiological studies must be interpreted with care and more studies are needed to better understand the possible causality between nutrition and dementia. Nutrition is a complex domain in which many factors are involved. For example, a moderate consumption of alcohol could be a marker of a healthy diet, as suggested in a study that showed that wine drinkers ate more food rich in antioxidant vitamins and unsaturated fatty acids (164). Also, education could be involved in the relationship between nutrition and dementia since highly educated subjects generally have a healthier diet, as shown in other studies (165-166). Furthermore, even if many of the results are adjusted for potential confounding factors, it is difficult to dissociate the impact of other factors that were not systematically taken into account, such as social environmental or circumstance of the meals. However, there is increasing evidence that poor nutritional habits are associated with a higher risk of dementia.

WEIGHT LOSS IN ALZHEIMER'S DISEASE

Cross-sectional studies show that demented elderly weigh less and have a lower body mass index compared to cognitively intact elderly (167-169). Up to 50% of institutionalised demented patients are assumed to suffer from malnutrition (170-171). In particular, subjects with Alzheimer's disease (AD) have been identified to be at high risk for PEM (169,171,172-175). Weight loss might be a "signal event" that occurs before or at the time of diagnosis of AD (176-177). Even

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though weight loss is present in the early stages, the risk tends to increase with the severity and progression of AD (178). Weight fluctuation seems to be frequent in AD (179). The aetiology of weight loss in demented patients is still unclear and is probably multifactorial. Potential factors contributing to weight loss are; inability to prepare and eat foods (180), impaired olfaction and taste, behaviour problems like agitation, restlessness (181-183) and wandering, (184), increased energy expenditure, inflammatory components of the disease and presence of co-morbid medical illness. Difficulty with feeding and weight loss become major issues in the care of almost all demented patients in the later stages of the disease. Within eight years of onset of AD, 50% of patients need help with feeding or artificial nutrition (185).

Olfactory causes
Pathological changes appear first in the olfactory system and may occur years before the onset of cognitive impairment (186). As a result of declining smell perception, appetite may be depressed, which subsequently may result in weight loss. Since olfactory ability is affected very early in AD the question arises of whether measures of olfactory ability could possibly aid in the identification of AD. Most of the early studies of olfactory perception in AD reported losses in the ability to identify, recognise, and detect odours. A recent meta-analysis of the published papers on olfactory functioning in AD concluded that severe deficits occur in three olfactory domains: identification, recognition and threshold with a trend towards somewhat better performance on threshold measures in comparison with recognition and identifications tasks (187). In addition to cognitive measures, measures of smell ability may also differentiate at-risk from not at-risk individuals (188).

Atrophy of the mesial temporal cortex
The mesial temporal cortex (MTC), which is involved in feeding behaviour and memory, is affected in the primary stages of AD and continues to be a site of major AD pathology as the disease worsens. Grundman, et al showed that in AD a low body mass index correlates best and specifically with atrophy of the MTC (189). They suggested that there is a connection between limbic system damage and low body weight in AD.

Inflammation
Inflammatory processes in the brain are thought to be of aetiological importance in AD. Increased levels of tumour necrosis factor (TNF)α and other pro-inflammatory cytokines in plasma and in cerebrospinal fluid are reported from patients with AD (190-192). Higher circulating TNFα may be derived from the local CNS inflammatory reaction in AD and may account for anorexia and weight loss. Cytokines may inhibit feeding by acting on the gastrointestinal system or indirectly on the central nervous system. The interaction by inflammatory activation and catabolic processes leading to anorexia and cachexia was first established in cancer diseases but has now been found to be an important factor in many chronic disorders. Anti-inflammatory treatment that reduces TNF and other cytokine activity may prevent cachexia (193).

Energy intake in AD
A majority of the studies that have assessed the daily energy intake in institutionalised and non-institutionalised AD patients suggest that the patients have an adequate energy intake (170,194-200). The most common method to assess daily energy intake was a 3-day weighed food record.

Energy expenditure

The most commonly employed methods to measure resting energy expenditure (REE) are indirect calorimetry and the doubly-labelled water method that measures total energy expenditure (TEE). A majority of studies in this field suggest that there is no increased energy expenditure or any hypermetabolic state in AD that can explain weight loss (201). Metabolic rate or daily energy expenditure have not differed between AD patients and healthy controls when normalised for body composition and physical-activity related energy expenditure (197). Measured rates of resting and physical activity energy expenditure are generally lower in AD patients because these individuals are usually small and have less metabolically active tissue (199). Given the fact that the disease activity seems to fluctuate, it is suggested that patients with AD might experience periods of elevated energy expenditure associated with weight loss. Total daily energy expenditure rather than REE should be the target of future studies on body weight regulation in these patients and should be performed during the dynamic phase of weight loss. Further studies with larger samples are needed. It will be important to evaluate how the new drugs, i.e. AChEIs used in AD-patients, affect weight and appetite. These drugs seem to improve behavioural symptoms and stabilise cognitive function (202). However, they may show adverse effects, related to dose, such as nausea, vomiting, diarrhoea, dyspepsia and anorexia (203).

A better understanding of the possible relationship between cytokine activity and energy intake may create new possibilities for preventing weight loss in AD patients (204). Weight loss should not be considered inevitable in AD patients. There is evidence that adequate nutritional support can stabilise weight and significantly decrease mortality rate. Much of the work on nutrition and dementia has focused on why weight loss occurs rather than on interventions that may promote weight maintenance or gain.

NUTRITIONAL TREATMENT OF SUBJECTS WITH COGNITIVE DECLINE

Oral supplements

Weight gain and its effect on nutritional parameters was seen in an RCT by Carver and Dobson where 46 psychogeriatric patients were included. Half of the group was given ONS of 600 kcal/day for 12 weeks resulting in a weight gain of 3.5 kg, while the control group maintained a stable weight. No evaluation of functional capacity, cognitive function or mortality was reported (205). In a Dutch psychogeriatric nursing home, Wouters-Wesseling, et al performed a double-blind, placebo-controlled, 12-week intervention study, in 42 patients aged ≥60, with BMI <23 for men or <25 for women. ONS providing 270 kcal/day resulted in a significant improvement of weight (2.2 kg), homocysteine, vitamin B1, thiamine diphosphate (TDF), vitamin B6, vitamin B 12, folate and vitamin D in the intervention group (206). In a study by Gregorio, et al, 25 of 80 AD patients randomly selected to receive ONS for 12 months, showed higher levels of albumin, iron, zinc,beta-carotene and MNA score than the control group. Mortality was lower (16% vs 22.7%) and the number of infectious events (47% vs. 66%) in the intervention group as was the number of days in bed (207).

Intervention with additional vitamins and minerals

Abalan, et al studied the effects of supplements on cognition in a randomised controlled pilot-study of 29 patients with dementia disorders. Fifteen individuals received vitamins, minerals and liquid supplements for 105 days. Fourteen subjects served as controls. At the end of the study the treatment group was reported to have a significant improvement in MMSE (+3.5 from a mean MMSE of 11.5

at start) compared to the control group (-2.7 from a mean of 9.7 at start). Effects on weight, food intake or other nutritional parameters were not reported (208). In a randomised, double-blind, placebo-controlled trial, 96 apparently healthy men and women aged >65 were randomly allocated to receive a daily supplement of trace elements and vitamins or a placebo for 12 months. At follow-up the supplemented group showed a significant improvement in almost all cognitive tests (P< 0.001 to 0.05). An increase in MMSE from 18 to 28 points was noted (<0.01) (209). However, in a small group of elderly with cognitive decline, a study by Baker, et al saw no effect on cognitive function after a 1-year intake of a high-dose vitamin and mineral supplement, despite elevated blood vitamins (210). In a controlled and blind study from Spain, ONS were given with (intervention group =23) or without micronutrient supplementation (control group=21) to patients with mild AD (MMSE 19-20) for 6 months. All patients received ONS (500 kcal/day) two times daily. The micronutrient enhancement showed no benefits to cognitive function in the intervention group but, interestingly, serum cholesterol decreased. As in other populations the ONS resulted in an increased energy intake (211).

Environmental factors improving food intake

The effects on ordinary food intake when an aquarium was placed in the diningroom were studied in 62 residents in dementia units for 16 weeks. Fish tanks were placed in the dining areas of two units and a scenic ocean picture was used in the control unit. There was an increase in weight in the aquarium group (P<0.000) whereas the scenic ocean picture had no effect on food intake or weight (212). An interesting study from the UK describes changes made over 6 years on a long-term ward for twenty 70-year old women with dementia. They had been residents on the ward for at least 4 of the 6 years. None of

the patients scored more than 3 on MMSE and initially patients were thin, mean BMI <18, with various feeding problems. A range of texture-modified meals was developed for dysphagic patients and a finger foods menu was developed to prolong the independence of those patients who could no longer remember how to use eating utensils. This menu also allowed food to be consumed while patients were wandering and at times other than fixed meals. Snacks were also introduced. Weight gain was noted and mean BMI increased from 19 to 25 in six women after 6 years (213).

It seems important to stimulate all senses of the person with dementia. In an intervention trial Ragneskog, et al investigated the effect of dinner music on food intake and symptoms such as depressed moods, irritability and rest-lessness. They concluded that dinner music, particularly soothing music, can stimulate demented patients in a nursing-home ward to eat more (214-215). The music reduced irritability, fear-panic and depressed moods. Enhanced lighting and reduced noise seem to improve food intake in AD units (216).

Ethical considerations

Nutritional therapy in severely demented subjects may raise ethical questions, especially when given to terminally ill subjects who may not benefit from the treatment (217-218). However, problems in eating and drinking present challenges at every mealtime from the first moment a patient needs help with meals. Studies that have focused on the way nurses deal with feeding problems found that they had difficulty interpreting refusal-like be-haviour and that their interpretations differed (219-221). It is stressful for the caregivers when the patients are no longer able to speak and make their wishes clear, and conflicts between caregivers and families are common. It is advisable to enable staff to learn from colleagues who have more experiences with patients who

are difficult to feed and to open a discussion of individual patients with professional colleagues and the patient's family. Successful nutritional care demands the expertise and commitment of a range of professionals and disciplines.

Ethical issues are important and must be considered during the different stages of the disease. Patients with mild to moderate dementia are likely to benefit from nutritional support and care. Since weight gain is likely to improve quality of life and well-being, the nutritional needs of this group of patients should be met as with any other group of chronically ill patients. However, in patients who have reached the final stage of dementia, when it is considered that nutritional support no longer benefits quality of life, the focus should be on the patient's comfort (218).

EDUCATION

Effects of nutritional education for staff and care takers

Malnutrition and insufficient nutritional care given to elderly people in municipal care and in hospitals has been highlighted in Sweden over the past 15-20 years. To address these problems, extensive lectures and nutrition education courses for care staff have been provided. Education is regarded as a cost-effective way of improving the ability of nursing staff to ensure adequate food intake for residents and in increasing nurses' and care staff's knowledge of nutrition. However, studies evaluating the results of nutrition education interventions are rarely reported in the literature. A couple of studies exist, and they report little or modest effects from education intervention for care staff.

Twenty nursing assistants answered a 15-item multiple-choice test before and after a 4-hour training session. Teaching strategies included discussions, audiovisual presentations, experimental exercises and role-playing. A slight improvement was noted in some question, but scores on pre- and post-tests did not differ significantly (222). The authors concluded by suggesting individual teaching of nursing

assistants, as they work with residents with repeated feedback, and informal nurse-led problem-solving sessions to discuss difficulties and challenges encountered during daily nutrition care instead of classroom teaching. In a study by Christensson, et al, nutritional education and a nutritional programme were performed in three intervention residential units (223). The staff at five other units were controls. A total of 176 nursing staff participated. The nutritional programme consisted of study circles including 8-10 members, on 5 occasions within three months. At follow-up one-year later it was concluded that education and implementation of a nutritional care programme appeared to have little impact on the attitudes of care staff, but the majority of the staff had positive attitudes towards nutritional nursing care. Registered nurses responded with more positive attitudes, than nurse's assistants. This might be a result of a higher level of education. Perry, et al found that even though education had no apparent impact on the level of nurses' knowledge of nutrition, it resulted in a more critical understanding and insight into the nutritional situation on the ward (224). Some studies have addressed questions about knowledge and attitudes among nurses in hospitals and nursinghomes. They report that many nurses lack sufficient nutritional knowledge to assess nutritional concerns of elderly residents (225). Many nurses had difficulty raising the priority of nutrition above other nursing activities (226).

Knowledge and attitudes are closely linked to each other, and consequently education programmes can have some impact by altering attitudes (227). Nutritional education courses given to nursing staff in rehabilitation and long-term care resulted in more flexibility and individual care of the patients (228). A similar pattern was found among nursing staff caring for severely demented patients, who found feeding easier when they

understood the nature of the patients' behaviour (229). Social influence and group norms are also important to consider and, according to Goffman, it is the staff working in an institution who frame the routines, roles and norms restraining the ongoing activities (230).

Education programmes to elderly subjects

A literature search of articles dated 1990-2003 on nutrition interventions and nutrition education for older adults aged >55 found 25 out of 128 studies that met certain requirements (231). The inclusion criteria were community-based inter-vention articles with measurable outcomes or evaluation components. Several studies were not included in the review because no significant intervention effects were reported. All studies were focused on "healthy eating" and on a "healthy lifestyle" and many of them included younger elderly. Overall, increased nutrition knowledge was the most successful outcome reported, whereas behaviour change and/or positive biochemical or anthropometric outcomes were quite variable. Age did not appear to be a limiting factor in increasing one's knowledge.

Positive outcomes appeared more probable when nutrition messages were limited to one or two and were simple, practical, and targeted to specific needs. Studies that provided nutrition education to motivated people or addressed older adults' health concerns were generally more successful. Several theories of behaviour modification were used to design interventions, particularly in the more recent studies.

AIMS OF THE STUDY

The main objectives of this thesis were to assess

- the nutritional status and cognitive function
  - in elderly people living in service flat (SF) complexes and to evaluate the effect of education programmes to SF care staff (study I, II).
  - in residents of group living for the demented (GLD) and to study the effects of oral nutritional supplementation and nutritional education of care staff (study III).
- nutritional status, short-term effects of adapted nutritional routines and possible relationships between weight, weight change and cognitive function in patients admitted to in-ward diagnostic examination of cognitive impairment (study IV).
- long-term mortality in relation to dementia diagnosis and nutritional status (study IV).

PATIENTS AND METHODS

SUBJECTS AND STUDY DESIGNS

Study I was performed in an service flat (SF) complex south of Stockholm. Twenty-eight (81± 7 years, 75% women) of 108 residents agreed to participate. To evaluate how representative these 28 participants were, 20 subjects (82 ± 5, 75% women) randomly chosen from the group of 65 pensioners who did not participate in the study were interviewed. In study II the participants were 80 out of 115 residents from two SF complexes, denoted SF-Intervention (I) and SF-Control (C), located in two suburbs south of Stockholm having similar demographic and socio-economic structures. Of 53 eligible residents in SF-I, 37 residents (84±7 years, 73% female) agreed to participate, while the corresponding numbers in SF-C were 43 out of 62 (82±7 years, 67% female). The residents of SF-I and SF-C had lived in the SF for 5 (2-8) and 3 (2-6) (median, 25-75th perc) years, respectively. In studies I and II (SF-I), nutritional education programmes (see below) was offered to the care staff and follow-ups were performed 5-6 months later.

In study III, residents of two different units of group-living for the demented (GLD) participated. The two GLD units were adjacent to the above-mentioned SF-I and SF-C. The need for care (see below) was the same in the two units. All residents were invited to participate in the study. The subjects that did not participate abstained due to the wishes of their relatives. An intervention took place in one of the group-living units, denoted GLD-I, where 22 of 23 residents (83 years, 82% females) participated. Fourteen of 18 residents (85 years, 93% females) in another GLD were controls (GLD-C). Before referral to GLD, the residents had been diagnosed with dementia as depicted in **Table 1**.

Co-morbidity was classified as cardiac (9 subjects), neurological/psychiatric (8) or

pulmonary (3). Five participants had more than one major disease and other diagnoses were found in 5 subjects. The rest (6) did not suffer from any other chronic illness. Two residents had diabetes; otherwise none of the residents had a special diet. The intervention in GLD-I consisted of an education programme for the care staff (see below) and oral supplements to the residents. Two 200 ml oral supplements (410 kcal/1720 kJ) were given daily over 5 months. A juicy supplement, Addera® (Semper AB), was given between meals in the afternoon. A balanced supplement, Komplett näring® (Semper AB), was given in the evening when the prescribed drugs were distributed. The care staff used a protocol where they registered the intake of the drinks.

In study IV, 231 individuals (80 ± 7 yrs, 65% women) consecutively admitted for in-ward investigation of cognitive function between October 1994 and June 1996 were included. The patients were referred from the greater southwest Stockholm area. The majority were referred to the clinic by their general practitioner and considered not capable of being examined as outpatients. Co-morbidities were registered. The patients were served food by educated staff in a homelike dining-room. Only whole-fat dietary products were used. Nutritional and cognitive status were followed during the hospital stay. Seven years later mortality data were obtained and registered from the Swedish population records.

NUTRITIONAL ASSESSMENT

Body Mass Index (BMI, weight (kg)/height $(m)^2$) was calculated. Height was measured in a standing position, using a horizontal headboard. Height in bed-bound residents was measured in a stretched position lying in bed with an un-stretchable measuring tape. Triceps skin fold (TSF) was measured using a Harpenden Skinfold caliper and arm muscle circumference (AMC) was calculated according to Jelliffe (70) in study I and II. The measurements were

made between the acromion and the olecranon on the non-dominant arm. An average of three recordings were calculated. Muscle strength in the dominant hand was measured using a Harpenden Grip Strength Dynamo-Meter® in study I,II and recorded as the better of two trials. The measurements were made by trained dieticians.

Moreover, in studies I-II the Subjective Global Assessment (SGA), described in the introduction, was used. We made further adaptations of the SGA for the assessment of older subjects by assessing weight changes over the course of 1 year, instead of 2 weeks and 6 months, respectively. Furthermore, we added fatigue, depression, constipation, chewing and swallowing difficulties to the symptom list, and we added locomotory difficulties under the heading of physical capacity. In addition, the residents in studies I and II classified their appetites using a visual analogue scale (VAS, 0-10) where 1=poor and 10 =very good) and they were interviewed about their eating habits.

To classify the participants as well-nourished, malnourished or at risk of becoming malnourished in study III, a nutritional score index (NuSc) was calculated from the outcome in the nutritional parameters BMI, TSF, AMC, albumin, transferrin and IGF-I. Values within the reference range were scored as 0 and values under the reference range as 1. The points in the six variables were compiled into the NuSc (0–6). NuSc 0 was arbitrarily chosen to indicate a well-nourished state, NuSc 1–2 risk for PEM and NuSc $\geq$3 denoted PEM.

Serum concentrations of albumin, transferrin (study II,III), vitamin B12, haemoglobin (Hb) and s-folic acid (study IV) were analysed as biochemical indicators of nutritional status. The routine methods and reference ranges of the Laboratory of Clinical Chemistry at the hospital were used. C-reactive protein (CRP, Hitachi 917, Boehringer-Mannheim, Germany) was measured to determine any active inflammatory activity, reference value <10g/l (study I-III). Furthermore, the anabolic mediator serum insulin-like growth factor-I (IGF-I) was analysed (study I-III) with a commercial radio-immunoassay after acid ethanol extraction (Nichols Products Corp., San Juan Capistrano, Calif., USA).

ASSESSMENT OF COGNITIVE FUNCTION

Mini mental state examination
In studies I-IV, the cognitive function was assessed using the Mini Mental State Examination (MMSE). This has been the most widely used screening test for simple, rapid assessment of cognitive impairment for almost 30 years. It has a high level of sensitivity and specificity for identifying cognitive decline (232) and it is recommended by several organisations as a routine screening measure for identifying cognitive impairment in clinical practice and research (233-234). It is not a diagnostic test for dementia, which requires as described below, several different examinations. The scores follow the changes in cognitive state when and if patients recover, and it is suitable for initial and repeated measurements. It has a high reliability when tested by multiple examiners.

The MMSE addresses seven cognitive performance areas and can give a maximum of 30 points. The different areas are: orientation to place (5 points), orientation to time (5 points), registration (3 points), attention and concentration (5 points), recall (3 points), language abilities (8 points) and visual construction (1 point). A score of $\geq$24 is considered normal, at least for those with a ninth grade education or more. Interpretation of an MMSE score should take into account education and physical impairment.

Clinical Dementia Rating scale
In study III, the degree of dementia was further assessed using the Washington

University Clinical Dementia Rating (CDR). This has been in use since 1977 in the Memory and Aging Project at Washington University, St Louis. It has been used in assessing the natural history of AD and has been extensively evaluated (235-238). It has proven useful as a longitudinal measure of the course of AD. The CDR is derived from a semi-structured interview with the patient and an appropriate informant and rates impairment in each of six cognitive categories or "boxes" (memory, orientation, judgment and problem solving, community affairs, home and hobbies and personal care) on a five-point scale in which none=0, questionable=0.5, mild =1, moderate=2, and severe=3 dementia. Each category is scored as independently as possible according to descriptions of impairment found in the CDR table. The overall CDR score (summary of boxes) is derived from the scores in the "boxes", using the same five-point scale of impairment. High overall CDR indicates severe dementia. The assessments were made by trained district nurses at the SF complexes.

Dementia diagnoses (study IV)

Dementia diagnoses in study IV were based on the DSM-IV criteria (110) after a complete dementia assessment had been performed including: a physical examination, neuropsychological evalua-tion, assessments of activities of daily living (ADL) and instrumental ADL (IADL), laboratory tests, electro-cardiography and electroencephalography recordings and a computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. Gottfries-Bråne-Steen scale (GBS) and Montgomery-Åsberg depression rating scale (MADRS) were also included in the investigation. The diagnoses were settled by the responsible ward physician.

ACTIVITY IN DAILY LIVING AND NEED OF ASSISTANCE

The participant's ability to manage activities of daily living (ADL), i.e. bathing, dressing/undressing, using the toilet, movement, transfer, continence and eating, were assessed according to the Katz ADL index (239). This index is graded as: A=independent in all functions, B= dependent on help in one function, C-F=dependent on help in 2-5 functions, and G=dependent on help in all six functions.

The SF residents (study I, II) were assessed by a senior local welfare official regarding their need for assistance, using a scale ranging from 0 (no help at all) to 8 (total dependence). Finally, the participants in studies I,II were asked to estimate their mood according to a VAS (0 = very sad – 10 = very happy).

STAFF EDUCATION AND QUESTIONNAIRE

Staff at the SF complexes attended 9 (study I) and 12-hour (study II-III) nutritional education programmes on several occasions. The education programme was compulsory for all staff at the SF. Dieticians, physicians, and external care staff gave lectures on malnutrition in the elderly, food and nutritional requirements, dental care, how to detect swallowing difficulties and how to change the consistency of food. Problems in eating connected with conditions like dementia, Parkinson's disease and stroke were elucidated. Lectures were combined with practical exercises, such as calculating BMI, making and testing nutritional drinks, thickening or enriching drinks of various types, and trying foods with changed consistencies.

The subjects of the care staff at the SF complexes (study I-III) answered a questionnaire at start and after 5-6 months. The questionnaire reflected whether the subjects were aware of the residents' weights, appetites and preference of food consistency, and if the residents ate alone or in company. They were also asked if

they thought they could influence the residents' food purchases. The care staff stated their assessment of the importance of nutrition in various diseases using a VAS scale (0, low – 10, high). Finally, the questionnaire contained a description of fictitious patient cases with fixed alternatives.

Table 1. Age, cognitive and functional status at baseline in elderly individuals living in two units of Group Living for the Demented (GLD). I= intervention unit, C= control unit.

	GLD (all) n=36	GLD-I n=21[1]	GLD-C n=12[1]
Age, yr	84 (4)	83 (4)	85 (4)
Sex, n/%, female	31/86	17/81	12/100
Type of dementia n /%			
Alzheimer's disease	8/22	6/29	1/8
Vascular dementia	7/20	4/19	2/17
Unspecified Dementa	21/58	11/52	9/75
CDR			
Degree of dementia, n/%			
No dementia (0)	-	-	-
Questionable dementia (0.5)	1/3	1/5	-
Mild dementia (1)	12/34	5/24	5/46
Moderate dementia (2)	10/29	6/28	4/36
Severe dementia (3)	12/34	9/43	2/18
Median (range)	2 (0.5-3)	2 (0.5-3)	2 (1-3)
Total score (0-18)	11.9 (4.6)	12.3 (5)	11.4 (4.6)
MMSE (0-30)	9.0 (6.2)	9.0 (6.6)	8.5 (6.2)
ADL, median (range)	E (A-G)	E-F (A-G)	D (A-G)

Mean (SD) if not stated otherwise. CDR=Clinical Dementia Rating Scale, MMSE=Mini Mental State Examination, ADL=Activities of Daily Living.
[1] Participants that completed the study.
No significant changes were found between the groups.

STATISTICS

Data are presented as mean $\pm$ SD or median (25th–75th percentile). To analyse the variations between two groups of residents, the Student's t-test, the Mann Whitney U-test and Chi-2 test were used in accordance with the type and distribution of the variables. To analyse variations between the diagnosis groups in study IV, one-way ANOVA, Kruskall Wallis one-way analysis of variance by ranks and Chi-square (X^2) tests were used in accordance with the type and distribution of the variables. For multiple comparisons, the Fisher LSD post hoc test was used. Possible changes at follow-up were evaluated by Student's paired t-test or Wilcoxon's Matched Pair Test. For correlation analyses, Pearson's and Spearman's correlation coefficients were calculated depending on type and the distribution of the variables. Multiple regression analyses were performed to evaluate possible independent relationships between the variables.

In study IV, logistic regression was performed to evaluate the prognostic values of different variables for 7-year mortality. For the statistical analyses, co-morbidity was dichotomised; i.e. no or mild and severe co-morbidity. For survival analysis we used Kaplan Meier and Log rank tests. The Statistica® software package (Statsoft, OK, USA) was used for the statistical calculations.

ETHICS

All investigated subjects received oral and written information before consenting to participate. Relatives of the demented individuals (study III) received written information and were asked to give their consent. All the studies in the project were reviewed and approved by the local ethics committee and conformed to the Helsinki declaration.

RESULTS

Nutritional status in SF residents (study I, II)

The mean BMI was just above the reference limit in study I and close to the upper reference range in study II (**Table 2-3**). None of the participating SF residents in study I displayed a BMI <20, whereas this was found in 13 (16%) of all SF residents in study II. There was no statistical significant difference between the participants and the "non-participants" in study I, but BMI tended to be somewhat lower in those residents and 11% had BMI <20. According to SGA, 11 % and 7% out of 28 SF residents in study I, and 21% and 13% of the 80 participating residents in study II, were assessed as being at risk for malnutrition and as malnourished, respectively. Weight loss exceeding 10% was found in 40% of the participants (study I) and in 52% (study II) when current weight was compared with highest recalled weight.

Hand grip strength (HGS) was related to AMC (r=0.6, P<0.01) but not to BMI (study I) and in study II, HGS correlated to weight (r=0.47, P<0.0001), haemoglobin (r=0.45, P<0.0001) and s-albumin (r=0.31, P=0.006). In residents with reduced ADL functions HGS were 15.1 ± 1.5 kg compared with 24.1± 2.2 kg (P<0.05) in those with full functional status (study I). In study II, HGS correlated negatively to ADL-function (rho =-0.32, P=0.004) and need for assistance (rho =-0.34, P=0.004). HGS also correlated to MMSE (rho=0.42, P=0.0001).

The biochemical nutritional indices were normal in both study I and II and did not differ between groups at start in study II. Serum IGF-I correlated with TSF (r= 0.45, P<0.01) but not with any other nutritional variables in study I. In study II s-IGF-I correlated to s-transferrin (rho=0.24, P=0.035) and to BMI (r=0.22, P=0.05).

The residents' self-assessments of their nutritional situation (study I, II)

One-fourth of the residents in study I reported chewing and swallowing difficulties, and roughly 50% in study II reported eating difficulties, where chewing and swallowing problems dominated (23%). Approximately 70 % in both studies were able to prepare and cook their own meals. On average the SF residents (study I and II) assessed their appetites as good, but 11% (study I) and 7% (study II) stated that they had a poor appetite.

Cognitive and functional status (study I, II)

On average, MMSE was 24 (study I) and 23 (study II), and 41% and 50% respectively had MMSE less than 24, suggesting impaired cognitive function. BMI correlated with MMSE (r= 0.43, P<0.03) in study I but not in study II (rho=0.05). Approximately 75% (study I) and 70% (study II) were ADL-independent at the start but 7 participants (28%) in study I and 25 subjects (31%) in study II had a Katz index >A. The average need for assistance was 2 among the participants in study I. Corresponding figures in study II were 3 (SF-I) and 2 (SF-C), respectively (ns).

Effects of care staff education - care staff (study I, II)

After the education programme, significantly more of the care staff in study I suggested enriched diets and food with different consistencies in the patient examples. Nine of 24 of the staff returned the questionnaire both times. In study II, the education programme seemed to raise the staff's awareness slightly, but no significant improvement was seen compared with the staff of the other SF complex. Seventeen of 25 care staff in SF-I, and 13 of 20 in SF-C filled in the questionnaire on both occasions. According to the test results on the fictitious patient case, staff knowledge appeared to improve (P=<0.05) (study II), without a significant difference between the two SF complexes.

Effects of care staff education – residents (study I, II)

The nutritional status of the residents in both studies (I and II) had not deteriorated at the 5-6 month follow-ups (**Table 2-3**). In study I, an increase of BMI was noted in the men, i.e. from 26.6 ± 3.1 to 27 ± 3.4, and of serum albumin from 38.7 ± 3.1 to 41.2 ± 3.5 g/l in all (P<0.01). Study II included a larger group of residents, and the possible effects of the nutritional education programme were evaluated under more controlled forms. At follow-up, no change in weight or BMI was observed in either of the two SF complexes. A decrease in serum albumin was noted in SF-C and a rise of serum transferrin found in both groups. SGA indicated that more subjects were classified as well-nourished (SGA A) and fewer as severely malnourished (SGA C) in SF-I, while no similar trend was observed in SF-C.

The ADL capacity remained unchanged in the SF residents in study I, but deteriorated in both groups of SF residents in study II. No positive changes in MMSE were noticed in the residents at follow-up in study I and II.

Effects of oral nutritional supplements and care staff education in residents of group living for the demented (study III)

A BMI ≤ 20 was found in 19% of the participants; 44% had a BMI ≤ 23 at start. According to the NuSc, two-thirds of the residents in both units were classified as malnourished or at risk for PEM. The means of anthropometric and biochemical values were within the normal range in both GLDs. BMI was found to correlate with MMSE (r=0.43, P<0.01). The weight of the residents in the intervention group increased by 3.4 ± 3 kg (P=0.001) at follow-up, whereas the weight remained unchanged in the control group (**Table 4**). Cognitive function was low at the start in both groups, i.e. MMSE ~9, and no apparent positive effect of the nutritional intervention was

seen. In addition, there was a deterioration of the ADL functions in both groups (**Table 5**).

Relationship between nutrition, cognition and mortality in patients admitted for diagnostic examination of cognitive impairment (study IV)

The mean BMI was in the normal range (23.3 ± 4), as were the biochemical indices, and they did not vary with the diagnoses. A BMI <23 was noted in more than half of the 231 patients. Weight and MMSE correlated weakly ($r = 0.18$, P< 0.01) at inclusion. The mean MMSE for the various diagnosis groups varied from 13.7–16.4, except for patients diagnosed as MCI. Fifty per cent had MMSE <17 points.

The distribution of the dementia diagnoses is presented in **Table 6.** For example, AD was diagnosed in four of 10 patients. Co-morbidities were found in 81% of the patients and varied among the dementia diagnoses groups (P< 0.01). Most frequent were cardiovascular disorders, which were present in about half of the patients and not unexpectedly in 70% of the subjects diagnosed as VaD. Almost one-third of the patients diagnosed as having AD did not have any other ongoing disease.

During an average 3-week hospital stay, the weight increased by 0.5 kg (P<0.001); the greatest increase (0.7 kg) was seen in patients with AD and VaD. Concurrently, an increase in MMSE of 1 point was noticed (P<0.001). However, changes in weight and MMSE did not correlate. A BMI <23 seemed to predict shorter 7-year survival (OR 3,95% CI 1.3-6.7), even after adjustment for age, gender and co-morbidity (**Fig 1**). The type of dementia diagnosis or the degree of cognitive impairment were not related to mortality in this group of patients.

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Table 2. Anthropometric and biochemical variables in pensioners living in service flats.

	All participants at start (n = 28)	Re-examined participants (n = 25) At start	6 months	Reference value
Body mass index (kg/m²)				
men	26.6±3.1	26.6±3.1	27.0±3.4*	20-25
women	25.6±3.2	25.6±3.2	25.4±3.4	19-24
Triceps skin fold thickness (mm)				
men	10.5±2.3	10.5±2.3	10.0±2.6	>6
women	20.8±10.7	22.5±10.4	22.5±10.6	>10
Arm muscle circumference (cm)				
men	26.4±2.0	26.4±2.0	26.5±1.8	>21
women	21.5±2.8	21.7±2.9	22.0±3.3	>19
Grip strength (kg)				
men	21.3±10.3	22.2±10.4	21.1±11.1	
women	37.2±5.1	37.2±5.1	36.6±5.1	
	16.0±4.1	16.3±4	15.1±5.4	
Serum albumin (g/l)	38.7±3.1	39.1±3.0	41.2±3.5**	35-46
Serum haemoglobin (g/l)	142.4±13.1	144.1±13.8	140.3±13.4	130-165
Serum Insulin-like Growth Factor-I (µg /l)	139.1±52.7	142.2±53.3	140.9±45.7	71-290 (≥55 yr)
Appetite (VAS 1-10)	7.5±3.0	7.9±2.8	7.4±3.4	
Subjective Global Assessment, median	A	A	A	
A (n)	23	23	22	
B (n)	3	1	2	
C (n)	2	1	1	
Mini Mental Test (0-30)	23.9±3.4	24.2±3.2	24.9±3.2	30
Mood (VAS 1-10)	6.3±2.1	6.4±2.2	5.4±2.8*	
Activity of Daily Living, median	A	A	A	

VAS=Visual Analogue Scale (1-10). Appetite: 1=no appetite, 10=good appetite, Mood: 1=sad, 10=happy.
Subjective Global Assessment: A=well-nourished, B=possible malnutrition, C=serious malnutrition.
Activity of Daily Living, A–G=independent to totally dependent. *=p<0.05, **=p<0.01.

Table 3. Anthropometric and biochemical variables, cognitive and functional status and mood in individuals living in service flats (SF) at baseline and after 5 months.

	SF-all, (n=80) At start	SF-Intervention (n=30) 0	5 months	P1	SF-Control (n=41) 0	5 months	P1	P2
Weight	63±15.2	65.2 ± 18.8	65.5 ± 19.1		62±12.7	62 ± 12.7		
Body mass index (kg/m^2)	24.3 ± 4.9							
men		28.2 ± 6.2 [a]	28.4 ± 6.1		23.4 ± 3.4 [a]	23.4 ± 3.5		
women		24.2 ± 5.4 [b]	24.2 ± 5.3		23.8 ± 4.8 [b]	23.8 ± 4.8		
Hand grip strength (kg)								
Men	30.3 ± 9.1	26.7 ± 9.3	24.5 ± 9.1	<0.01	33 ± 9	32.8 ± 8.5		<0.05
Women	15.7 ± 6.9	11.9 ± 5.1	10.5 ± 6.3	0.05	18.9 ± 6.3	19.7 ± 4.3		<0.05
Serum albumin (g/l)	40.1 ± 4.2	38.9 ± 4.1	38.6 ± 3.7		40.9 ± 4.2	39.7 ± 4.2	<0.05	
Serum transferrin (g/l)	2.2 ± 0.4	2.2 ± 0.3	2.2 ± 0.3	<0.05	2.3 ± 0.5	2.4 ± 0.5	<0.05	
Serum hemoglobin (g/l)	130 ± 16	130 ± 15	129 ± 15		130 ± 16	130 ± 15		
Serum vitamin B12 (pmol/l)	381 ± 284	309 ± 161	329 ± 156		402 ± 313	419 ± 317		
Serum Insulin-like growth factor-I (µg/l)	105 ± 48	102 ± 51	103 ± 51		109 ± 49	106 ± 52		
Appetite (VAS 1-10)	7.2 ± 2.9	6.9 ± 2.7	6.5 ± 2.7		7.8 ± 2.8	7.7 ± 2.6		
Subjective Global Assessment, n (%), A	52 (66)	17 (57)	20 (69)		31 (76)	30 (73)		
B	17 (21)	8 (26)	8 (28)		7 (17)	7 (17)		
C	10 (13)	5 (17)	1 (3)		3 (7)	4 (10)		
Mood (VAS 1-10)	5.3 ± 2.5	5.9 ± 1.9	5.9 ± 2.4		5.2 ± 2.8	5.2 ± 2.0		
MMSE	22.5 ± 5.2	21.2 ± 5.5	21.3 ± 6		23.2 ± 5.2	24.1 ± 5.3		
ADL, (median, 25-75th perc.)	A (A-B)	A-B (A-D)	B (A-E)	0.05	A (A-A)	A (A-B)	0.001	

P1 refers to changes over time within the groups. P 2 refers to difference in change over time between the groups.
[a] In total 22 men; 9 in SF-I, 13 in SF-C, [b] In total 49 women; 21 in SF-I, 28 in SF-C.
MMSE = Mini Mental State Examination. ADL = Activities of Daily Living

Table 4. Anthropometric and biochemical variables in elderly individuals living in two units of group living for demented (GLD) at start and after 6 months. GLD-I = intervention unit, GLD-C = control unit.

	GLD all, n=36	GLD-I, n=21[1]			GLD-C, n=12[1]				Ref. value
		0	6 mo	p1	0	6 mo	p1	p2	
Weight	58.8 (10.8)	55.4 (10.4)	58.8 (11.2)	p<0.001	62.2 (8.2)	61.9 (10.4)		p=0.003	
M[2]	64.1 (15.2)	58.6 (10.2)	60.8 (10.7)		-	-			
F[3]	57.9 (10)	54.6 (10.6) *	58.3 (11.5)	p<0.001	62.2 (8.2)	61.9 (10.4)		p=0.004	
BMI, kg/m^2	23.1 (3.9)	22.2 (4.1)	23.5 (4.4)	p<0.001	24.6 (2.9)	24.5 (3.8)		p=0.003	20-25
Se-albumin, g/l	39.7 (3.9)	40.6 (4)	38.6 (4)	p=0.010	38.4 (3.4)	35.8 (3.2)	p=0.012		35-46
Se-CRP, g/l	<10	<10	<10		<10	<10			<10
Se-transferrin, g/l	2.1 (0.4)	2.2 (0.3)	2.1 (0.3)		2.1 (0.5)	2.1 (0.5)			1.9-3.3
Se-Hb, g/l	132 (12)	133 (14)	132 (9)		128 (11)	124 (12)	p=0.055		130-165
Se-B12, pmol/l	454 (305)	542 (343)	579 (349)		332 (192)	332 (173)			110-600
Se-IGF-I,[4] µg/l	126 (61)	145 (70)*	140 (76)		100 (36)	96 (36)			83-209[4]
NuSc[5] (0-6), n/%									
0 (well-nourished)	11/31	8/38	8/38		2[5]/18	2/19			
1-2 (at risk for PEM)	20/58	11/52	8/38		7/64	6/54			
≥3 (PEM)	4/11	2/10	5/24		2/18	3/27			

Mean (SD) if not otherwise stated. M=male, F=female, BMI=Body mass index, CRP=C-reactive protein, IGF-I=insulin-like growth factor-I, NuSc=nutrition score, PEM=protein-energy malnutrition.
*refers to changes between the groups at start, p<0.05.
p1 refers to changes over time within the groups, p2 refers to difference in change over time between the groups.
[1]Participants that completed the study. [2]Four in GLD-I, 0 in GLD-C. [3]17 in GLD-I, 12 in GLD-C.
[4]10th-90th percentile in 31 healthy controls >75 y of age. [5]NuSc was possible to calculate in 11 of the GLD-C residents.

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Table 5. Cognitive and functional status in elderly individuals living in two units of Group Living for Demented./GLD), at start and after 6 months. I= intervention unit, C= control unit.

| | GLD-I (n=21) | | | GLD-C (n=12) | | | |
	0	6 mo	p¹	0	6 mo	p¹	p²
CDR Scale,							
median (range)¹	2 (0.5-3)	3 (1-3)	p=0.04	2 (1-3)	2 (1-3)	p=0.03	p=0.054
CDR Scale							
total score (0-18)	12.3 (5)	14.7 (3.6)	p<0.001	11.4 (4.6)	13.3 (3.6)	p=0.037	
MMSE (0-30)	10.9 (6.2)	8.4 (5.9)	p=0.014	10.2 (5.3)	10.7 (5.3)		p=0.01
ADL (A-G),							
median (range)	E (A-G)	F (B-G)	p=0.018	D (A-G)	E (B-G)	p=0.093	

Mean (SD) if not stated otherwise. CDR=Clinical Dementia Rating Scale, MMSE=Mini Mental State Examination, ADL= Activities of Daily Living.
¹ categorized in 5 groups (0 = no dementia, 0.5 = questionable dementia, 1= mild dementia, 2 moderate dementia, 3 = severe dementia),
P¹ refers to changes over time within the groups.
P² refers to difference in change over time between the groups.

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Table 6. Demographic, anthropometric and biochemical variables at start in 231 older subjects undergoing examination of cognitive function.

Diagnoses	All	AD	VaD	MCI	Others	Mixed	Ref values	P [a]
n (%)	231	93 (41)	33 (14)	38 (17)	47 (20)	19 (8)		
Age, years	80±6.8	80.5±7.1	80.5±6.8	78 ± 7.6	79 ± 6	82 ± 4.4		
Female, n (%)	151 (65)	67 (72)	20 (61)	24 (63)	26 (55)	14 (74)		
MMSE, 0–30 p	16.6±6	14.8±5.7	16.4±4.7	22.8±4.8	16.4±5.6	13.7±4.2		<0.001
Weight, kg (n=228)	61.6±12.3	60.7±12.5	60.6±13.9	62.2±10.6	65.2±12.3	57.1±10.4		
BMI, kg/m^2 (n=208)	23.3±4.1	23±4.4	23.6±4.3	23.4±3.6	23.8±4.2	22.5±3.7		
BMI <23, n (%) (n=208)	108 (52)	43 (51)	17 (55)	18 (50)	18 (47)	12 (67)		
Se-albumin, g/l (n=216)	35.5±4.6	35.8±4.7	34.5±3.6	36.3±4.6	35.4±5.2	34.6±3.7	35–46	
Se- B$_{12}$, pmol/l (n=212)	384 ± 398	356 ± 337	427±495	386 ± 402	412 ± 439	373 ± 375	110–600	
Se-folic acid, nmol/l (n=195)	14.7±14.7	15.3±15.9	10.3±5.6	15.7±16.5	14.3±9.2	18.9±24.7	> 4	
Se-Hb, g/l (n=215)	129±15	130±14.5	129±15	130±14.4	128±19.5	129±10.5	115–145	

Mean ± SD, median (25–75th perc) or n (%). AD = Alzheimer's disease, VaD = Vascular Dementia, MCI = Mild cognitive impairment, Others = Other diseases: Dementia Not otherwise specified (n = 29); depression, confusion or psychiatric disease (n = 4) Parkinson-dementia (n = 2), Normal Pressure Hydrocephalus (NPH) (n = 5), Frontotemporal dementia (n = 4) and examination of cognition (n = 1), Mixed = dementia with both AD and VaD components. MMSE = Mini Mental State Examination. BMI = body mass index. [a] = differences between the groups at start (ANOVA).

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Fig 1. Seven-year survival in individuals with various cognitive disorders and BMI <23 and ≥23, respectively (Kaplan–Meier curves and Log Rank Test).

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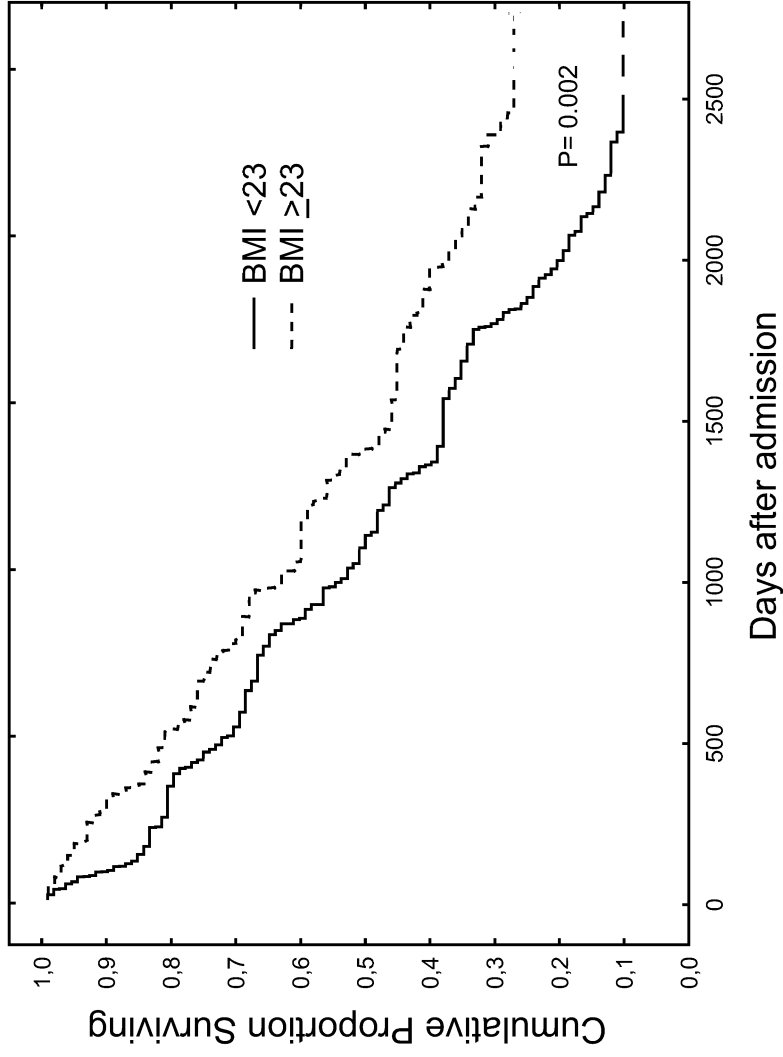
GENERAL DISCUSSION

STUDY I AND II

The SGA assessments indicated that one in five SF residents (study I) and one in three (study II) was possibly or seriously malnourished. On average BMI was slightly higher in the residents in study I (26 in women and 27 in men) than in the study II population (BMI 24). A weight loss of 10% or more, when current weight was compared to reported highest weight, was more common in study II. Most of the subjects were independent of care need and a majority of the residents were capable of cooking and preparing food. These studies indicate that the nutritional status varied greatly within the SF complexes and that the proportion of malnourished residents was higher in study II.

Most of the subjects in study I applied voluntarily to participate after informational meetings about the study, whereas the SF residents in study II, after receiving written information, were personally invited. Thus the participants in study I may have represented the most healthy and most active residents in the SF. In one study, of 349 Swedish SF residents, the mean BMI was 24 (22), which is in line with our findings in study II. The study of Saletti et al and study II were performed later than study I, which may indicate that the SF population is becoming more frail and chronically ill.

Cognitive function assessed by MMSE was related to BMI in study I but not in study II. However, MMSE correlated to other nutrition-related variables like hand-grip strength. Four of ten in study I and half of the study II residents demonstrated cognitive impairment. Given the fact that mainly the frail elderly in need of care move to community funded sheltered housing, it is likely that the prevalence of dementia will be high. In a representative sample of 85-year-olds, living in Gothenburg, dementia defined according to the DSM-III-R criteria, was diagnosed in one-third of 494 individuals (240).

Educational effects on residents

The major aims of study I and II were to evaluate whether a limited education effort could affect the SF staff's awareness of and knowledge about nutrition for the elderly, and to see whether the staff training might improve the nutritional status of the residents. The nutritional status in the residents in study I and II did not show any objective improvements at the 5-6 month follow up. However, by SGA the SF-I residents showed an improvement that was not observed in the SF-C residents. The impact of an isolated staff education programme may not be strong enough to show an effect with the instruments for objective nutritional assessment that were used. Maybe the residents had benefited more of an intervention programme addressed more directly to themselves, instead of focus the educational efforts towards the care staff. The majority of the subjects in both SF-studies were independent and took care of themselves, and would likely have been able to attend an education programme about nutrition in the elderly. In a review of nutrition education to the elderly by Sahyoun et al, it was found that age was not a limiting factor in increasing one's knowledge. Positive outcomes appear to be more probable when nutrition messages were limited to one or two, were simple and practical, and targeted to specific needs. Sahyoun concluded that nutrition education to older adults may prevent or delay the spiral toward ill health and disability (231).

Efforts were made in both studies to engage the staff in the restaurants to participate in the education classes and to facilitate for the restaurants to offer energy-enriched food and provide desserts. Since the restaurants did not belong to the SF-complexes, they were not obliged to take part in the programmes. Unfortunately, no one of the restaurant staff attended.

Possible limitations, especially of study II, may be that the SGA and the interviews

were performed by two different dieticians, one at each SF complex. However, the SGA classification technique has demonstrated a high reproducibility among numerous assessors (91,241). Moreover in study II, as well as in study III, two different nurses performed the assessments of ADL, MMSE and CDR at SF-I and GLD-I, since one district nurse changed jobs in the middle of the study. However, also MMSE is considered to be reliable when performed by multiple examiners (232).

Educational effects on staff

The effects of the nutrition education programme on the SF care staff were modest (study I and II). In study II the nutrition knowledge appeared to increase in both groups of care staff, but there was no difference noted between the two SF-complexes. In study II, the fact that the staff in the SF-C was aware of the ongoing nutritional programme in SF-I, and the presence of a dietician who performed the nutritional assessments might have influenced the results. In a prospective RCT of ONS in malnourished elderly in the community, it was suggested that simply providing control subjects with the attention of a dietician had a placebo effect, which was enough to cause them to increase their dietary intake. This occurred despite the fact that the dietician acted as a researcher and did not give dietary advice to control group subjects (95). Moreover, it must be taken into consideration that the number of staff persons completing the questionnaires at both occasions was low. Malnutrition and insufficient nutritional care given to elderly people in municipal care was frequently reported in the Swedish media during this period, which also may have influenced the care staff.

In a recent report, a nutritional education programme based on study circles, with a focus on existing and problematic nutritional issues, did not affect the staff's attitudes (223). The authors concluded that the intervention was not strong enough, corroborating the difficulties in performing

and evaluating similar studies. Perry L has suggested that when changing nursing practice in nutritional care, increasing knowledge only is not sufficient. Insight into the influence of group norms and identification of individual and situational characteristics are important and must also be addressed (242). Although not corroborated by these studies, it is still reasonable to believe that nutritional education of care staff may, especially in sheltered accommodation with more dependent residents, reduce the risk of malnutrition in the residents. Perhaps a combination of nutritional supplements and an education programme to care staff and residents, would be beneficial.

SGA and MNA

Both study I and study II were performed before MNA was established in Sweden. Today MNA is more often used than SGA in assessing nutritional status in elderly people, at least in municipal care. Several investigators suggest that SGA is more useful in detecting elderly residents with established malnutrition, while MNA identifies subjects who need preventive nutritional measures (46,90). Since early detection of subjects at risk for malnutrition is urgent, MNA is suggested to be first option in assessing elderly people (92). Still, both methods are used and validated in the assessments of older people (241,243-244). The methods correlate well (46), even though MNA has a more global approach, covering not only nutrition but also cognition, mobility and morbidity, whereas SGA focuses more on nutrition issues. SGA, was used in studies I and II, combined with BMI, TSF, hand-grip strength, biochemical markers of nutrition, and MMSE to assess cognitive function.

Hand-grip strength correlated with nutritional markers, which is in accordance with several previous reports (74-75,78). It also correlated to MMSE and ADL. Therefore, hand-grip strength measurements may be useful in the nutritional and functional assessment of elderly people.

STUDY III AND IV

Weight gain in subjects with dementia

A BMI less than 23 was noted in about half of the study participants in studies III and IV. BMI did not vary with the diagnoses in study IV, which is in accordance with some (170,196), but not all studies (245). In study III, a similar comparison was not possible, due to the small groups and the large proportion of residents with unspecified dementia diagnoses. BMI and MMSE correlated in study III, and a weak correlation between weight and MMSE was found in study IV.

The intervention in study III, providing training to care staff and oral supplements to the GLD-I residents, resulted in a significant weight gain. Nine months after the supplements were withdrawn, a significant decrease in weight was noted, suggesting that the supplements given to the residents had a stronger impact on the weight evolution than the nutritional training given to the care staff. No positive effects on cognition or on functional capacity using MMSE, CDR or Katz' ADL index in the GLD-I residents were found after this intervention.

After an average hospital stay of three weeks, a slight increase in weight and in MMSE score was noticed in the 231 patients undergoing investigation of their cognitive function (study IV). However, these improvements did not correlate. The subjects with a BMI <22 at start gained more weight than those with a BMI ≥22, indicating that the patients who were underweight at admission had the best potential for responding to the adapted nutritional routines in the ward.

Much of the work on nutrition and dementia has focused on why weight loss occurs, rather than on interventions that may promote weight maintenance or gain. In studies III and IV, we found that weight gain was possible in people with mild (study IV) and moderate (study III) dementia. It has been suggested that "nutritional intervention" during periods of weight loss may be of value, and a 2-year prospective study of 362 community-living AD patients resulted in a substantial weight gain in some of these seniors (168). Institutionalised elderly people with dementia can maintain their weight and improve their survival if sufficient calories are provided (174,246-247). Individualised strategies regarding the eating environment and diet may enhance body weight and therefore nutritional health (248,182). Sufficient numbers of professional nutrition staff to support food intake is important (247). Weight was reported to be maintained in a special care unit, regardless of pacing and other clinical characteristics of the patients (249). Furthermore, it was found that clinical dietician time and an enhanced menu, designed to be individualised for ambulatory people with dementia, promoted weight gain.

Weight gain may be viewed upon as a surrogate variable for other, more clinically relevant outcome variables. Thus, future research should try to measure other outcome variables than weight gain and also focus on functional and clinical outcomes. For example, a study by Gregorio et al (207) found reduced morbidity and mortality in institutionalised patients with AD after one year of nutritional supplements.

The majority of nutritional intervention studies in subjects with dementing disorders focus either on cognition or nutrition as outcome variables. The question of whether cognitive effects may be achieved from nutritional treatment in weight-losing patients with dementia disorders is not resolved.

The gain in weight that was observed in study III was not related to improved ADL or cognitive function assessed by Katz, and MMSE or CDR, respectively. A more sensitive instrument than the Katz ADL-index may have been able to register the small signs of improvement that were noted by relatives and staff. It should be noted that the residents already showed a pronounced decline in cognitive capacity; whether fortified nutrition in subjects with milder

forms of dementia has other effects remains to be studied. Somewhat contrasting findings is recently reported. A nutrition education programme, with 9 one-hour sessions over the course of one year, was performed in 151 day-hospital patients with dementia (MMSE 15 at start) and their caregivers. Seventy-four patients served as controls. The mean weight of the intervention group increased, whereas it decreased in the control group. A slower rate of cognitive decline was also noted in the intervention group (P=<0.05). The caregiver's knowledge of nutrition and of dementia increased after the education programme (P<0.005) (250)

However, the results of studies III and IV indicate that it is difficult to affect the cognitive function in subjects with cognitive impairments by improvments of the nutritional status in general. The studies are small and it cannot be excluded that positive effects may be achieved if larger samples of patients were included, as in the study of Riviere et al. As discussed in the introduction, the use of particular nutrients, e.g. omega-3 fatty acids or anti-oxidative agents, may be another possible way of interfering with the dementing process by nutrition that needs to be evaluated.

Body mass index, dementia and long term mortality

Seven year mortality in relation to BMI and dementia diagnoses was evaluated in study IV. A BMI ≥23 was found to be associated with an increased survival rate, independently from age, male gender and co-morbidity. Co-morbidity, but neither type, severity or duration of dementia disorder, did predict length of survival. The degree of cognitive impairment, evaluated by MMSE was not associated with long-term mortality in the present study. The type of dementia diagnosis did not have a significant impact on mortality in this study but the patients that were diagnosed as suffering from "other dementia diseases" tended to have the highest mortality. High age and the presence of severe co-morbidities most likely were stronger determinants of mortality than the

dementia disease in itself. The finding that a BMI ≥23 in people with dementia predicted longer survival is in agreement with data from geriatric patients with other types of chronic disease (41-42). To identify older patients at risk for being underweight, a cut-off of BMI ≤23 has been suggested (43). Half of the subjects in study IV and one of four in study III had a BMI below this level, and one-third of the SF-residents in study II had a BMI <22. Several studies implicate that BMI 25-30 in elderly subjects may be prognostically favourable (41,251). In healthy elderly BMI has slightly increased during the last decades, and in a large reference group of healthy Swedish woman and men in their 80s in the beginning of the 1990s, values of 26 and 25.5 respectively were noted (252).

On the other hand, obesity in middle-age, defined by a BMI >30, is found to be a risk factor for Alzheimer's disease (119). The risk increases if other cardiovascular risk factors like hypertension and hyper-lipidaemia are added. Gustafson et al recently reported that obesity in 70 year-old women was a risk factor for dementia later in life (125). Nutritional factors should not be neglected in the prevention and treatment of dementia, especially in Alzheimer's disease. Underweight in frail elderly with or without cognitive dysfunction should be treated and every effort should be taken to prevent it. Obesity, now also suggested as a risk factor for AD, should also be avoided, especially in middle-aged people.

ASSESSMENTS OF FOOD INTAKE

No assessments of dietary intake were performed in any of the current studies, but some comments will be made upon the methods that have been used in the studies referred to in the introduction.

Food frequency questionnaires (FFQ) are used to estimate an individual's intake of nutrients in epidemiological studies. This method requires patients to recall and report their consumption of a large number (150-200) of food items, including the usual serving size and frequencies of consumption

at specified intervals over a general time period. Accurate and complete FFQ responses certainly require sustained motivation, attention, and memory (253). Validation of FFQ with multiple food records (254) or 4-day food record (255) together with 24-hour urinary nitrogen showed good agreement. Weighed-food and estimated record intakes yielded higher correlations with urinary nitrogen and urinary potassium than estimates from FFQ (256). To confirm the different hypothesis suggested by epidemiological data, well-designed intervention trials, as well as observational investigations, based on larger cohorts, studied over longer periods of time, with several methods for assessing intake of certain nutrients are needed.

To assess whether the weight loss in demented patients is related to low dietary intake, a number of studies assessing food intake have been done using various methodologies. Several studies have used a 3-day diary or 3-day weighed food record. Only a few studies have used the method of weighing food and reweighing the uneaten portion (7-days). In hospitalised patients, staff-administered records are most common and due to intra-and interpersonal variations, food and fluid intake should be recorded for several days before the patients' intakes can be classified. A 7-day dietary record routine based on standardised portion sizes and household measuring seemed to have a good reproducibility in assessing the intake of energy and fluids in geriatric patients (257). Repeated measurements of food intake were also performed by Sandman et al (170). Since weight fluctuation occurs in AD patients it may be possible that episodic low energy intake are not recorded by records such as 3-day food. Ultimately, food weighing for at least 3 or more days during the week, in different periods of the year, during weight loss and weight-stable periods, would be the most reliable method of measuring dietary intake.

It must also be held in mind that the measurement itself may influence the staff so that patients receive better care during the periods of dietary recording (170,195).

CONCLUSIONS

- Impaired nutritional status was found in
- one of three to five service flat residents and in
- about half of group-living subjects with dementia
- A reduction in cognitive function was found in almost half of the service flat residents.
- Nutritional status and cognitive function correlated in groups of service flat and group-living residents as well as among subjects undergoing diagnostic examinations for dementia.
- A limited nutrition education programme to care staff
- had no clear positive effect on the nutritional status of SF residents 5-6 months later
- did not lead to overt improvements in the knowledge of the personnel.
- The combination of education of care staff and oral nutritional supplements to residents of group-living for demented resulted in a weight gain, whereas the gain in weight was not related to an improvement in ADL function or cognitive function.
- Body mass index (BMI) did not vary with dementia diagnoses.
- Three weeks of hospital stay with adapted nutritional routines was associated with weight gain and improved cognitive function, whereas there was no correlation between the weight gain and the cognitive improvement.
- A BMI <23 seemed to predict seven year mortality in individuals with cognitive failure.
- Mortality rate did not differ with dementia diagnosis or degree of dementia in subjects with dementia disorders.
- More studies are needed to determine the relationships between nutrition and cognition in elderly SF residents, as well as in elderly people suffering from dementia disorders.

IMPLICATIONS FOR FUTURE RESEARCH

- Effects of nutritional education programmes addressed to residents of service flats at risk for malnutrition needs to be assessed.
- In education intervention programmes, all groups of staff, e.g. the staff working in SF restaurants, should be included in the study.
- Mechanisms underlying weight loss in patients with dementia disorders need to be better understood.
- The possible beneficial effects of particular nutrients, e.g. omega-3 fatty acids, for patients with dementia disorders need to be further evaluated.

ACKNOWLEDGEMENTS

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