Dietary 'acid load' and self reported prevalence of hip fractures:
A population based, cross sectional study

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Det er kjent at syrebelastning, spesielt av uorganiske syrer, øker risikoen for osteoporose og benbrudd. På den annen side vil inntak av basedannende mat som grønnsaker og frukt redusere risikoen. I *Helseundersøkelsen i Oslo* inngår bl.a. spørsmål om lårhalsbrudd. I denne artikkelen er det undersøkt om selvrapportert prevalens av lårhalsbrudd er relatert til inntak av visse typer syre- eller basedannende mat og drikke. Odds ratio for selvrapportert prevalens av lårhalsbrudd økte hos personer med sjeldent inntak av *rå grønnsaker/salat*, dvs. ≤ 1-3 mot > 1-3 ganger pr. måned (OR=1,70; 95% CI=1,34–2,15; p<0,001), når det ble justert for alder og kjønn. 'Risikoen' for lårhalsbrudd var signifikant økt for personer med lavt inntak av *kokte grønnsaker*; OR=1,45; 95% CI=1,07–1,98; p=0,02. For dem som anga lavt inntak av både rå og kokte grønnsaker var OR=2,07; 95% CI=1,35–3,18; p<0,001. Inntak av *frukt* ≤ 1-3 ganger pr. måned vs. > 1-3 ganger pr. måned ga en OR for lårhalsbrudd på 1,76; 95% CI=1,29–2,40; p<0,001. For dem som anga sjeldent inntak av både rå og kokte grønnsaker, og av frukt var OR=2,31; 95% CI=1,41–3,78; p<0,001. Sjeldent inntak av *ost* (alle typer) økte 'risikoen' for lårhalsbrudd (OR=1,94; 95% CI=1,42–2,65; p<0,001). Assosiasjonene mellom sjeldent inntak av de nevnte kostfaktorer og økt risiko for lårhalsbrudd ble funnet hos både menn og kvinner. Det var ingen signifikant sammenheng mellom inntak av cola (eller annen brus) og selvrapportert prevalens av lårhalsbrudd. Resultatene kan passe med tidligere rapporter om at inntak av grønnsaker, frukt og bær er gunstig for skjelettet, kanskje via redusert syrebelastning eller økt tilskudd av kalsium, vitamin K og/eller fiber.

INTRODUCTION

It is generally agreed that nutritional factors are important for the development of osteoporosis, a major predisposing condition for fractures. Among several negative factors for bone formation are sodium, protein, caffeine, oxalate, fibre, phytate, and increased acid load, whereas e.g. calcium and vitamin D seem to be dietary bone promoting factors. Also alkali buffers, whether bicarbonate, vegetables, or fruits can reverse the urinary calcium loss (1-4). In ovariectomized rats a variety of salads, herbs and cooked vegetables have been shown to beneficially influence bone metabolism (1).

In the present work we have examined whether data of the Oslo Health Study would fit the hypothesis that frequent intake of foods regulating the acid-base balance would affect the prevalence of self reported hip fractures.

MATERIAL AND METHODS

In 2000-2001 the Oslo Health Study was conducted under the joint collaboration of the National Health Screening Service of Norway (now the Norwegian Institute of Public Health), the University of Oslo and the Municipality of Oslo. The study population included all individuals in Oslo County born in 1970, 1960, 1955, 1940/41 and 1924/25. A total of 18770 individuals (45.9% of the invited) participated – in other words 8404 men (42.4%) and 10366 women (49.3%) attended the physical examination and/or filled in at least one of the questionnaires. For the five age cohorts the participation rates were 36.1, 43.7, 46.5, 55.4 and 53.2%, respectively. Baseline measurements included height, weight, waist and hip circumference, blood pressure, heart rate, and non-fasting blood tests to analyze serum total cholesterol, HDL-cholesterol, triglycerides, and glucose.

One self-administered questionnaire was part of the letter of invitation, whereas two supplementary questionnaires were handed out at the survey, and sent back in pre-stamped self-addressed envelopes. The questionnaires provided information on health status, symptoms, diseases and various aspects of health behaviour.

Up to two reminders were sent to the non-responders of the invitation to participate in the survey. The second reminder invited those living in the suburban parts of the city to mobile screening units parked in the neighbourhood of the invited. For further details, see: http//www.fhi.no/tema/helse-undersokelse/oslo/index.html. The study protocol was placed before the Regional Committee for Medical Research Ethics and approved by the Norwegian Data Inspectorate. The study has been conducted in full accordance with the World Medical Association Declaration of Helsinki.

Statistical analyses were done by SPSS 11.1. Using logistic regression, odds ratio and 95% confidence intervals were computed for the 'risk' of (self-reported) hip fractures and osteoporosis ('yes' or 'no'), for low vs. high frequency of intake of various food items and drinks. The food variables had 6 values for intake frequency: **1**=rarely/never; **2**=1-3 times per month; **3**=1-3 times per week; **4**=4-6 times per week; **5**=1-2 times per day, and **6**=3 or more times per day. For logistic regression analysis the variables were dichotomized into 'low' frequency, i.e. ≤ 1-3 times per month and 'high', i.e. > 1-3 times per month, after adjusting for age and sex. 'Crude mean intake frequencies' were calculated as the mean of all reported frequencies based upon the values given above. The food frequency questions do not allow calculation of 'true' intake frequencies, and no correction was made for variations in unit, e.g. intake rarely/never, per month, week or day. When appropriate, Student's t-test, ANOVA and Scheffe's test for multiple comparisons were used to compare mean values between groups. A significance level of 0.05 was used. SPSS 11.0 was used to produce the figures.

RESULTS

The number of subjects reporting hip fractures is shown in Table 1. For men the self reported prevalence (%) of hip fractures in the four age groups was 1.52, 1.03, 2.65, and 3.89. Corresponding values for women were: 0.85, 0.67, 1.05, and 6.15.

Crude mean intake frequency of **raw vegetables/salads** in subjects reporting hip fractures and 'controls' in the various age groups is shown in Figure 1. Note that the 'crude mean' is the mean of all reported frequency values (1-6, see methods), neglecting the variation, in unit (intake rarely/never, per month, week or day). Only in age group 59-60 the crude mean intake frequency of raw vegetables/salads was significantly lower in cases than in 'controls' (p<0.001).

The odds ratio for reporting *hip fractures* was significantly higher in subjects reporting a rare intake of raw vegetables (≤ 1-3 times per month) compared with subjects reporting a more frequent intake (> 1-3 times per month), after adjusting for sex and age: OR=1.60; 95% CI=1.26–2.03; p<0,001. Considering each age group separately, significant associations between low frequency of using raw vegetables/salads and increased self reported prevalence of hip fractures were obtained in age group 59-60 years (OR=2.35; 95% CI=1.45–3.81; p=0.001), and in age group 75-76 years (OR=1.43; 95% CI=1.01–1.99; p=0.003), but not in the two lowest age groups. Similar associations were found when analyzing each sex separately (data not shown). There was also a significantly increased odds ratio for reporting *osteoporosis* (OR=1.24; 95% CI=1.02–1.50; p=0.033) in subjects with a rare intake of raw vegetables, when adjusting for age and sex.

The odds ratio for reporting hip fracture was significantly increased in subjects with a rare vs. a high (i.e. ≤ 1-3 vs. > 1-3 times per month) reported intake of **cooked vegetables** (OR=1.79; 95% CI=1.34–2.38; p<0.001). Crude mean intake frequency of cooked vegetables in subjects reporting hip fractures and 'controls' in the various age groups is shown in Figure 2. There was an age related increase in the reported use of cooked vegetables (p<0.001). In all age groups the mean intake frequency of cooked vegetables was higher in 'controls' than in cases. Considering subjects reporting low intake of both raw and cooked vegetables vs. those with a higher frequency (as defined above) the odds ratio was OR=2.07; 95% CI=1.35–3.18; p<0.001 (hip fracture yes/no=232/13081). Similar associations were found when analyzing each sex separately (data not shown).

Table 1. Number of subjects answering yes or no to the question about hip fracture, by sex and age.

	Men		Women	
Age (years)	Yes	No	Yes	No
30	27	1754	19	2213
40+45	29	2797	24	3555
59-60	54	1982	24	2270
75-76	58	1434	122	1863

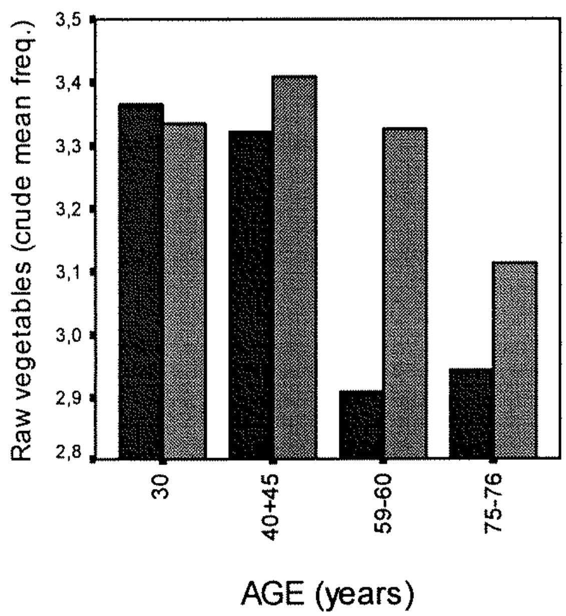

Figure 1. Crude mean intake frequency of **raw vegetables/salads** in subjects reporting hip fractures (black columns) and 'controls' (grey columns), by age. Note that the 'crude mean' is the mean of all reported frequency values, neglecting the variations in unit (rarely/never, times per month, week or day).

Crude mean intake frequency of **fruit/berries** in subjects reporting hip fractures and 'controls' in the various age groups is shown in Figure 3. There was an age related increase in the crude mean reported intake frequency of fruit/berries (p<0.001), most consistently for 'control' subjects. In all age groups, except in the lowest one, the mean intake frequency was higher in 'controls' than in cases.

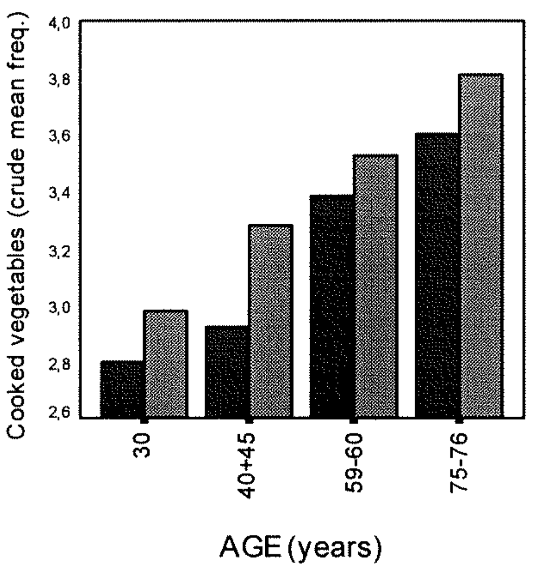

Figure 2. Crude mean intake frequency of **cooked vegetables** in subjects reporting hip fractures (black columns) and 'controls' (grey columns), by age. Note that the 'crude mean' is the mean of all reported frequencies, neglecting the variations in unit (rarely/never, times per month, week or day).

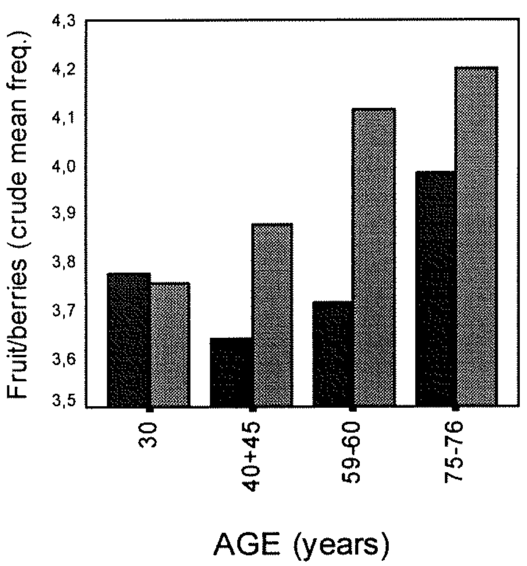

Figure 3. Crude mean intake frequency of **fruit/berries** in subjects reporting hip fractures (black columns) and 'controls' (grey columns), by age. Note that the 'crude mean' is the mean of all reported frequency values, neglecting the variations in unit (rarely/never, times per month, week or day).

Intake of fruit/berries ≤ 1-3 vs. > 1-3 times per month increased the self reported odds ratio for hip fractures (OR=1.71; 95% CI=1.27–2.31; p<0.001), when adjusting for age and sex. Results in the various age groups (adjusted for sex) were: 30 years (yes/no=45/3931), OR=1.01, 95% CI=0.45–2.29, p=0.980; 40+45 years (yes/no=53/6288), OR=1.89, 95% CI=0.99–3.64, p=0.055; 59-60 years (yes/no=77/4191), OR=2.19, 95% CI=1.23–3.89, p=0.008; 75-76 years (yes/no=172/3215), OR=1.60, 95% CI=0.97–2.62, p=0.065. Thus, the relationship between frequency of intake of fruit/berries and reported prevalence of hip fracture was significant only in age group 59-60 years.

Among subjects reporting rare intake of both raw and cooked vegetables, and at the same time rare intake of fruit we found OR=2.58; 95% CI=1.50–4.44; p=0.001 (hip fracture yes/no=207/11380).

Some **carbonated beverages**, especially cola, have been implicated in osteoporosis and bone fractures, due to their influence on the acid-base balance (5). In the Oslo Health Study there are questions about the use of cola, other carbonated beverages, and juice. In the present study we found no significant association between the prevalence of hip fractures and frequency of *cola* intake (≤ 1-3 vs. > 1-3 times per month); OR=1.03; 95% CI=0.66–1.60), p=0.893), *other carbonated beverages* (OR=0.66, 95% CI=0.40–1.09, p=0.104), the *mineral water Farris* (OR=0.93; 95% CI=0.60–1.43, p=0.732), or *fruit juice* OR=1.22, 95% CI=0.95–1.56, p=0.120). Rare vs. more frequent intake of potatoes (≤ 1-3 vs. > 1-3 times per month) was associated with increased odds ratio for reporting hip fractures (OR=1.79; 95% CI=1.34–2.38; p<0.001).

Also a high intake of **protein** has been suggested to negatively influence the development of osteoporosis due to the presence of sulphur containing amino acids which could be metabolized to produce sulphuric acid (6). Although this cross sectional questionnaire study does not give quantitative information about protein intake, we have considered the question about use of **cheese**, which is a source of both protein and calcium. Odds ratio for hip fractures in subjects reporting use of cheese (all types) ≤ 1-3 times per month vs. > 1-3 times per month was 1.94 (95% CI=1.42–2.65; p<0.001), when adjusting for sex and age. The odds ratios in the various age groups for reporting hip fractures related to a low vs. high frequency of using cheese were: age 30 years (yes/no=43/3927), OR=2.43, 95% CI=1.16–5.12, p=0.019; 40+45 years (52/6280), OR=2.52, 95% CI=1.29–4.93, p=0.007); 59-60 years (75/4193), OR=1.78. 95% CI=0.95–3.33, p=0.074; 75-76 years (173/3219), OR=1.72,95% CI=1.01–2.94, p=0.048.

Crude mean frequency of cheese use in the various age groups in subjects reporting hip fractures and 'controls' is shown in Figure 4. There was an age related increase in the frequency of cheese intake, and cheese was more frequently used in 'controls' than in hip fracture cases (except in age group 75-76 years).

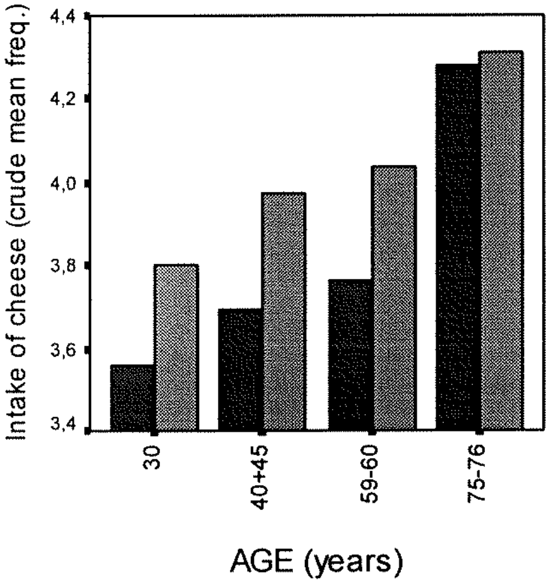

Figure 4. Crude mean intake frequency of **cheese** (all types) in subjects reporting hip fractures (black columns) and 'controls' (grey columns), by age. Note that the 'crude mean' is the mean of all reported frequency values, neglecting the variations in unit (rarely/never /times per month, week or day).

DISCUSSION

The present results seem to support the contention that intake of vegetables and fruit is beneficial for the skeleton.

Questionnaire information about disease prevalence could lead to erroneous conclusions. The self reported occurrence of hip fracture and osteoporosis in the present study is not validated. Conceivably, answers to the question about osteoporosis should be considered less reliable than the question about hip fracture. This contention is corroborated by previous reports (7,8).

It is pointed out that a crude measure of mean intake frequency was used in this report. The data do not allow calculation of intake frequencies using the same unit, since one response alternative was 'rarely/never'. 'Crude mean intake frequency' was calculated on the basis of the 6 values for frequencies (see Material and methods). Thus, the figures showing mean intake frequency do not reflect the correct mean intake frequency. If the variables were to be used as a measure of amount intake of particular food items this approach would seem inappropriate. However, 'frequency data' are not suitable to give information on the exact intake *amount*, even if the shown mean intake frequencies were true ones. In any instance, the crude means presented in this article would serve to illustrate variations in the intake pattern between those reporting yes or no to the question about hip fractures.

We wanted to see if the data of this cross sectional study would fit the hypothesis of an association between dietary acid load of the body and fracture (osteoporosis) occurrence.

The pH of blood is regulated within a narrow range of 7.35-7.45. In man life is not possible at pH < 7.0 or pH > 7.8, i.e. a hydrogen ion concentration above 0.100 or below 0.016 micromoles per litre (9). The carbonic acid-bicarbonate buffer system

$$CO_2 + H_2O \Longleftrightarrow H_2CO_3 \Longleftrightarrow HCO_3^- + H^+$$

is especially important. *Organic* acids consisting of carbon, hydrogen and oxygen have CO_2 and water as metabolic end products. Hence, surplus acid can be transported out via the lungs, without affecting the bicarbonate pool. Unlike this, *inorganic* acids give H^+ which will push the above equilibrium to the left, thereby lowering the bicarbonate concentration. Protons from these acids will mainly have to be excreted in the urine. Under normal conditions an acid load will produce a more acid urine. Protons can also bind to ammonia and HPO_4^{2-}, to be excreted in the urine as ammonium ions and $H_2PO_4^-$. To ensure electrical neutrality of the urine, anions will have to balance excretion of the cations. For example, phosphate is taken from the skeleton together with calcium ions. A large proportion of the inorganic material of the skeleton is hydroxy apatite, a crystalline calcium-phosphorus compound. Thus, in response to increasing the acid load, bone mass may be reduced upon release of calcium and phosphorus (3).

In general, a vegetarian diet will give a urine with pH > 7.0, i.e. a basic reaction. Thus, a high supply of fruit and vegetables in the diet will lower the acid load, thereby reducing the urinary loss of calcium. The finding in the present study of an association between a low frequency of intake of vegetables and fruit and increased occurrence of hip fracture would seem in keeping with a suggested calcium conserving effect of these food items.

In fact, as early as in 1931 Farquharson et al. (10) found that acute intake of acids like sulphuric acid, hydrochloric acid, and ammonium chloride lead to increased urinary calcium excretion in man. On the other hand, intake of bicarbonate gave reduced excretion. Chronic acid load in medical conditions is also associated with increased calcium excretion. Barzel and Jowsey (11) reported that, in rats, ammonium chloride (giving an acid reaction) added to the drinking water increased urinary calcium loss, followed by increased resorption of bone and development of osteoporosis.

It has been reported that increased intake of protein can give a more acid urine (6). Inorganic acids can be produced during protein catabolism, due to the presence of sulphur containing amino acids (2). As mentioned above, the kidneys will have to take care of the excess protons. A high protein intake has been hypothesized to promote fractures, based upon a positive correlation between the prevalence of fractures in women in various countries and the protein intake (12). There seems to be increased risk of fractures in people having a low intake of calcium and at the same time a high intake of animal protein (13). On the other hand, in elderly patients supplemented with calcium, protein appears to have a beneficial effect on bone health (14,15).

Cheese contributes positively to protein intake. This raises the question how a frequent use of cheese might be associated with hip fractures. However, cheese is also an excellent source of calcium, which is a required mineral for bone formation. The present results would suggest an apparent protective role of cheese against hip fracture, possibly being attributed to its high calcium and protein content. However, it is inappropriate to imply causal relationships in this cross sectional study, especially since the data do not give information on amount eaten.

Carbonated beverages are increasingly used in Norway, in particular among children and younger adults. The impact of these drinks on acid base balance probably should be different between organic acids found e.g. in juices, and beverages containing inorganic acid (*vide supra*). It has been previously reported that intake of cola, a soft drink containing phosphoric acid, is associated with increased risk of fractures in young females (5). Using cola as an alternative to milk would be expected to reduce calcium supply as well. The data of the present study appears not to be in support of an association between frequent use of cola (or other carbonated beverages) and hip fractures. Possibly, the age groups especially prone to hip fractures had not adopted a frequent use of cola during the several years preceding the incident, thereby avoiding a negative impact on bone.

In the rat, indigestible carbohydrates of plants, such as fructooligosaccarides, have been shown to increase intestinal calcium absorption, calcium balance, and bone mineral density (16,17). Among mechanisms of action are increased absorptive area of the large bowel produced by a high fibre content, and formation of short-chain fatty acids serving to promote calcium absorption in the colon. Also fibre components of fruits and vegetables could have such effects.

Green vegetables may also serve to retain calcium through their vitamin K content (18), thereby possibly explaining in part the observed association between frequent use of vegetables and reduced 'risk' of hip fractures. This suggestion is in line with other reports (19,20).

The present results are based upon a cross sectional study. Hence, conclusions about cause-and-effect associations would be inappropriate. Additionally, self reported outcome variables are unreliable. Moreover, in this type of study there are other differences than age *per se* when comparing one age group with another. In spite of these considerations, it is tempting to suggest that the present results are in favour of the view that frequent use of vegetables and fruit has a beneficial influence on the skeleton. Among possible mechanisms of action are reduced acid load, as well as increased intake of calcium, vitamin K and fibre.

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