RESEARCH ARTICLE

Mandibular inferior cortex erosion as a sign of elevated total serum calcium in elderly people: a 9-year follow-up study

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Objectives: The mandibular inferior cortex (MIC) classification that was determined by observing the mandible distally from the mental foramen in panoramic radiography can be considered to reflect bone loss in the jaws. The purpose of this 9-year study was to investigate whether there is a relationship between MIC condition and total serum calcium (TSC) in elderly Japanese people.

Methods: A total of 280 subjects aged 70 years at baseline (137 males and 143 females) took part in this longitudinal study design. TSC and dental panoramic radiographs were carried out at the baseline in 1998 and the final year in 2007.

Results: The results of the MIC measurement were divided into two groups according to changes in MIC after the 9-year study period, namely no change group and change group. A significant relationship was found in females but not in males between the MIC condition and the TSC. The regression showed that female subjects are 3.26 times more likely to have increased erosion of the inferior border of the mandible than male subjects after the 9-year study period.

Conclusions: These results suggest that an increase in erosion of the inferior border of the mandible was significantly associated with an elevated TSC after 9 years and only in females. *Dentomaxillofacial Radiology* (2014) **43**, 20130341. doi: 10.1259/dmfr.20130341

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Keywords: dental panoramic radiographs; mandibular inferior cortex; total serum calcium; elderly people

Introduction

There has recently been increasing interest in the mandibular inferior cortex (MIC) classification. The measurement of the MIC, which was originally devised by Klemetti et al,¹ was determined by observing the mandible distally from the mental foramen on both sides on dental panoramic radiographs. Some investigators have suggested that the MIC classification can be used to identify females who are at an increased risk of

osteoporosis.^{2,3} Other investigators have found significant associations between the MIC classification and the number of remaining teeth.^{4,5} Previously, we have reported the significant association between MIC classification and bone loss in the os calcis.⁶ The study showed that the MIC classification can be used in general dental practice to identify the suspected risk of osteoporosis and to refer patients to medical professionals to have further assessments for osteoporosis.

Other studies investigated regarding bone metabolic markers and bone minerals. The study of the MIC classification in relation to bone metabolic markers, such as serum bone-specific alkaline phosphatase (S-BAP) and urinary N-telopeptide cross-links of type I collagen

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(U-NTX) demonstrated a positive relationship. The MIC classification correlates more with U-NTX as a bone resorption marker than with S-BAP as a bone formation marker.⁷ Therefore, the MIC classification can be considered to reflect bone formation and bone resorption metabolism. Studies of bone resorption in relation to bone mineral showed that one of the bone mineral components that is strongly related is calcium. In the elderly, it is very important because of its crucial role in osteoporosis.⁸ In relation to drug interaction, adequate calcium in the bone is very important to obtain the maximal benefit from bisphosphonate therapy to allow for osteoblasts to deposit new bone mineral.⁹ However, the correlation of MIC with calcium, which is involved in most metabolic processes and provides mechanical rigidity to the bones, is still lacking evidence. Therefore, we conducted a study between MIC and total serum calcium (TSC) to investigate the relationship among these factors.

It has been shown that changes in metabolism are directly related to age, specifically that some bodily functions decline with advancing age. Some investigators have reported that many factors that influence bone metabolism, such as serum 25(OH)D and oestrogen status, are not significantly different until patients are more than 69 years old, and bone calcium decreases when a patient aged over 69 years of age gets older and TSC in the blood is not absorbed well.¹⁰ Therefore, it is necessary to evaluate subjects older than 69 years of age in large numbers to control confounding variables. We investigated the correlation between the eroded cortex of the mandible and the TSC in males and females in a longitudinal study design. We hypothesized that there might be a relation between the increased erosion of the inferior border of the mandible and the elevated TSC. The purpose of this 9-year study was to investigate whether there is a relation between MIC condition and TSC in elderly Japanese adults.

Methods and materials

Subject sampling

The examination protocol used for all subjects was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University (Niigata, Japan). A longitudinal study was conducted in older adults who reside in Niigata City, Japan. Blood measurements and dental panoramic radiographs were obtained at the baseline in 1998 and the final year in 2007. In 1998, 4542 Niigata citizens (2099 males and 2443 females), all of whom were 70 years old, were sent a written request to participate in the survey and were informed of the purpose of the survey. After two requests, 81.4% (3695) responded positively. After considering the availability of resources, examination appointments were arranged for 600 individuals. The subjects were randomly selected from eight areas in Niigata to have an approximately equal number of males (306) and females (294). Of the 600 participants

at the baseline, 272 dropped out after the 9-year study. 7 people were excluded because they did not want to undergo dental panoramic radiography, while 28 pairs of radiographs were excluded because the images of the MIC were not qualified either at baseline or the final years. Data from 23 subjects that did not provide information on TSC, total serum protein, serum phosphorus, number of tooth loss or smoking habits were also excluded. A total of 280 subjects, 137 males and 143 females, who did not take medication that might affect bone metabolism after 9 years of study participated in this study.

All subjects were Japanese, in good general health and did not require special care for their daily activities. None of the subjects had a history or current signs of systemic disease or was hospitalized or institutionalized. They filled out a detailed questionnaire, including questions about smoking habits. Blood serum variables (TSC, total serum protein and serum phosphorus) were measured at a commercial laboratory (BML, Inc., Tokyo, Japan).

In addition, physical activity and the number of remaining teeth at baseline and final years were measured to investigate the relationship with MIC condition after 9 years of study. We used the four physical fitness tests which were preceded by a medical examination:

1. Maximum hand-grip strength was measured using a Smedley hand dynamometer (DM-100s; Yagami Inc., Nagoya, Japan) in two trials for both the dominant and non-dominant hands. The score obtained was the best of the trials for both grip strengths.
2. Maximal isometric knee extensor strength was determined by a portable chair incorporating a strain gauge connected to a load cell. The subject sat on a seat in a vertical position that was adjusted so he or she sat comfortably with the leg hanging vertically and knees bent at 90°. The test was alternately performed twice on the right and left legs, respectively. Extensor strengths of the left and right leg were summed for this analysis.
3. Maximal leg extensor power was determined by an isokinetic dynamometer (Aneropress 3500; Combi Co., Tokyo, Japan). The subject was instructed to sit on the seat of the plate as fast as possible until his or her legs were fully extended. The body mass of each subject was applied as a resistance. The best score of five trials was used for this analysis.
4. Maximal stepping rate for 10 s was used as an index of agility using an industrial stepping rate counter (Stepping Counter; Yagami Inc.). The subject was instructed to step alternately as quickly as possible with each leg, while in a sitting position for 10 s. The stepping rates of the left and right legs were summed for this analysis.

The number of remaining teeth was recorded by two dentists using the blinded single-observer method.

Radiographic measurement of the mandibular inferior cortex

Subjects underwent dental panoramic radiography during their initial assessment. The position of the head was standardized as much as possible. Subjects were positioned in the panoramic unit in a way that the vertical line produced by the unit was aligned with the facial midline, and the horizontal line (Frankfort plane) was parallel to the floor. All panoramic radiographs were obtained using a Super Veraview X-500 (Morita Co., Tokyo, Japan) at 5–10 mA for 15 s; the tube potential varied between 60 and 80. We used speed group 200 screens (HG-M; Fuji Photo Film Co., Tokyo, Japan) and UR-2 film (Fuji Photo Film Co.). Measurements of the MIC was determined by observing the mandible distally from the mental foramen on both sides, and the results were divided into three groups (Class 1–3)¹ (Figure 1):

1. Class 1 (normal cortex): the endosteal margin of the cortex was even and sharp on both sides.
2. Class 2 (mildly to moderately eroded cortex): the endosteal margin showed semi-lunar defects (lacunar resorption) or appeared to form endosteal cortical residues on one or both sides.
3. Class 3 (severely eroded cortex): the cortical residues were clearly porous on one or both sides.

MIC classification was measured by one of the authors. The observer was trained by another researcher who had 4 years' experience of using the MIC classification. 100 randomly selected panoramic radiographs were reanalysed with a period of at least 1.5 months between the observations. Owing to the difficulty of standardizing the position of the head that leads to projection errors on the radiographs, the radiographs were taken by the same radiologist, a specialist in dental panoramic radiographs. Furthermore, the radiographs were interpreted and selected by the observer to avoid dubious radiographs specifically for the purpose of this study.

Statistical analysis

Initially, the subjects were divided into two groups according to their sex. The results of the MIC measurements were divided into two groups: those whose MIC classification did not change and those whose MIC classification changed after the 9-year study period (MIC condition). To evaluate TSC, means and standard deviations (SDs) at the baseline and the final year were used to characterize continuous variables. Statistical analysis between the MIC condition and TSC after 9 years was evaluated using the Student's *t*-test.

We also investigated other variables such as total serum protein, serum phosphorus and smoking habits. The statistical differences between males and females among MIC condition and smoking habits were evaluated using the χ^2 test and Fisher's exact test when applicable. Whereas, statistical differences among TSC, total serum protein and serum phosphorus were evaluated by the

Class 1: Normal MIC

Class 2: Mildly to moderately eroded MIC

Class 3: Severely eroded MIC

Figure 1 Mandibular inferior cortex (MIC) classification. Class 1: normal MIC; Class 2: mildly to moderately eroded MIC; Class 3: severely eroded MIC.

Student's *t*-test. Mean values at the baseline and follow-up year were used to evaluate the relationship of physical fitness and remaining teeth measurements with MIC condition after 9 years using the Student's *t*-test.

Finally, logistic regression analysis was performed to assess the relationship between MIC condition and TSC after 9 years, controlling for confounding factors. MIC condition was selected as the dependent variable, which was 0 for the group whose MIC classification did not change during the 9-year study period or 1 for the group whose MIC classification changed after the 9-year study period. TSC after 9 years, total serum protein after 9 years, serum phosphorus after 9 years, sex (0 if male,

Table 1 Characteristics of the study subjects

Characteristics	Male	Female	p-value
Subjects (n)			
No change in MIC classification after 9 years	113	94	<0.005 (χ^2 test)
Change in MIC classification after 9 years	24	49	
Total serum calcium after 9 years (mg dl ⁻¹) ^a	9.01 ± 0.3	9.14 ± 0.3	<0.001 (Student's <i>t</i> -test)
Total serum protein after 9 years (g dl ⁻¹) ^a	7.06 ± 0.3	7.15 ± 0.4	<0.05 (Student's <i>t</i> -test)
Serum phosphorus after 9 years (mg dl ⁻¹) ^a	3.38 ± 0.4	3.79 ± 0.3	<0.001 (Student's <i>t</i> -test)
Smoking habit (n)			
No smoking	98	142	<0.001 (Fisher's exact test)
1–10 cigarettes per day	15	1	
11–20 cigarettes per day	19	0	
21–30 cigarettes per day	2	0	
>31 cigarettes per day	3	0	

MIC, mandibular inferior cortex.

^aMean ± standard deviation.

1 if female) and smoking habit (0 if no smoking, 1 if current or previous smoker) were selected as independent variables. The level of significance was set at $p < 0.05$ for these tests. All calculations and statistical analyses were performed using STATA™ software (StataCorp, College Station, TX).

Results

The characteristics of the subjects are shown in Table 1. There were significant differences among MIC condition, TSC, total serum protein, serum phosphorus and smoking habit between males and females. The kappa values for intraobserver and interobserver agreement were 0.82 and 0.72, respectively. Based on the guidelines of the interpretation of kappa statistics performed by Landis and Koch,¹¹ the following categories were considered: <0.00 (poor), 0.00–0.20 (slight), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial) and 0.81–1.00 (almost perfect). The kappa value of intraobserver and

interobserver agreements was in the category of almost perfect and substantial, respectively. TSC at the baseline was 9.00 ± 0.33 mg dl⁻¹ for the study subjects and 9.02 ± 0.37 mg dl⁻¹ for the group who dropped out during the study. The difference between the two groups was not significant ($p = 0.383$; Student's *t*-test).

The description of the physical activity and number of remaining teeth related to the MIC condition after 9 years of study are shown in Table 2. At baseline, we found that there were significantly higher means and SDs of maximum hand-grip strength ($p = 0.002$), maximal isometric knee extensor strength ($p = 0.01$) and maximal leg extensor power ($p = 0.01$) in groups whose MIC classification did not change compared with those groups whose MIC classification did change according to the Student's *t*-test. Whereas, the follow-up year had significantly higher means and SDs only at maximum hand-grip strength ($p = 0.005$) and maximal isometric knee extensor strength ($p = 0.02$).

The distribution of the MIC classifications after the 9-year study period is shown in Table 3. The percentages

Table 2 Description of physical activity and number of remaining teeth related to mandibular inferior cortex condition after 9-year study

Description	No change in mandibular inferior cortex classification after 9 years	Change in mandibular inferior cortex classification after 9 years	p-value (Student's <i>t</i> -test)
Physical activity at baseline ^a			
Maximum hand-grip strength (kg)	34.9 ± 0.8	30.6 ± 1.2	$p = 0.002$
Maximal isometric knee extensor strength (kg)	53.5 ± 1.5	46.8 ± 2.1	$p = 0.01$
Maximal leg extensor power (W)	729.4 ± 23.4	626.3 ± 36.9	$p = 0.01$
Maximal stepping rate for 10 s (times/10 s)	78.6 ± 1.2	77.7 ± 1.9	NS
Number of remaining teeth at baseline ^a	22.6 ± 0.6	20.9 ± 1.1	NS
Physical activity at final year ^a			
Maximum hand-grip strength (kg)	33.5 ± 0.7	29.8 ± 1.2	$p = 0.005$
Maximal isometric knee extensor strength (kg)	30.2 ± 0.9	26.7 ± 1.3	$p = 0.02$
Maximal leg extensor power (W)	516.3 ± 21.4	459.2 ± 35.6	NS
Maximal stepping rate for 10 s (times/10 s)	81.8 ± 1.3	81.8 ± 2.1	NS
Number of remaining teeth at final year ^a	16.8 ± 0.7	15.1 ± 1.1	NS

NS, not significant.

^aMean ± standard deviation.

Table 3 Distribution of the mandibular inferior cortex (MIC) classification in female and male subjects after the 9-year study

<i>Subjects</i>	<i>MIC classification in 1998</i>	<i>MIC classification in 2007</i>
Males		
Class 1 ^a	127 (92.7%)	103 (75.2%)
Class 2 ^b	10 (7.3%)	34 (24.8%)
Class 3 ^c	0	0
Total	137 (100.0%)	137 (100.0%)
<i>p</i> -value	<0.001 ^d (Fisher's exact test)	
Females		
Class 1 ^a	69 (48.2%)	26 (18.2%)
Class 2 ^b	65 (45.5%)	102 (71.3%)
Class 3 ^c	9 (6.3%)	15 (10.5%)
Total	143 (100.0%)	143 (100.0%)
<i>p</i> -value	<0.001 ^d (Fisher's exact test)	

^aNormal MIC.

^bMildly to moderately eroded MIC.

^cSeverely eroded MIC.

^dThere were significant differences in the distribution of MIC classification after 9 years in both males and females.

of the MIC classification Classes 1, 2 and 3 in 1998 and 2007 were 92.7%, 7.3% and 0%, and 75.2%, 24.8 % and 0%, respectively, for males, and 48.3%, 45.5% and 6.3%, and 18.2%, 71.3% and 10.5%, respectively, for females. We found there were significant differences in the distribution of the MIC classifications between those in 1998 and those in 2007, both in males and females ($p < 0.001$; Fisher's exact test).

The mean and SD values for TSC in those whose MIC classification did not and did change after the 9-year study period were 9.00 ± 0.31 and 9.04 ± 0.29 mg dl⁻¹, respectively, for males, and 9.10 ± 0.26 and 9.21 ± 0.29 mg dl⁻¹, respectively, for females (Figure 2). In females, but not males, there was a correlation between increased erosion of the inferior border of the mandible and elevated TSC after the 9-year study period according to the Student's *t*-test.

The results of the logistical regression analysis are shown in Table 4. Subjects whose MIC classification did change were 4.82 times more likely to have increased levels of TSC than subjects whose MIC classification did not change after 9 years of study. Whereas, female subjects were 3.26 times more likely to have increased

erosion of the inferior border of the mandible than male subjects after the 9-year study period.

Discussion

To our knowledge, this is the first study to demonstrate an association between the MIC classification and TSC. Many factors contribute to bone metabolism not only in bone mineral intake but also in physical activity. The interaction between bone mineral intake and TSC is not fully understood, nor is the effect of TSC and physical activity on bone metabolism, but many investigators believe that adequate calcium intake and physical activity are critical issues for maintaining bone metabolism.^{12–14} To reflect bone metabolism, we used MIC conditions on a series of dental panoramic radiographs and investigated the relationship with TSC after 9 years.

The results of our study indicate that an increased erosion of the inferior border of the mandible was significantly associated with elevated TSC after 9 years and in females (Figure 2). These findings might be explained by the following reasons. The first possible mechanisms are related to calcium function, including calcium intake, absorption and excretion. It has been reported that calcium absorption decreases with age. This could be due to a decline in serum calcitriol, possibly because of declining renal function; a decline in gastrointestinal response to calcitriol;^{15,16} declining exposure to sunlight; or a decline in the capacity of the skin to synthesize vitamin.¹⁷ However, in healthy subjects, although calcium absorption may decrease with age, calcium excretion does not.^{18,19} This mechanism results in inadequate bone calcium absorption, while TSC becomes higher. Other investigators have reported that a lack of oestrogen in post-menopausal women prevents the absorption and utilization of calcium and is the single most important factor in the development of osteoporosis in older women.^{20,21} In this study, a relationship was found in females but not in males. In our opinion, the potential for an interaction between hormonal activity, diet and physical activity to influence bone metabolism is likely to be important. The ageing process plays

Figure 2 The relationship between mandibular inferior cortex (MIC) condition and total serum calcium after 9 years of study in males (a) and females (b). (a) There was no significant relationship between the MIC condition and the total serum calcium in males ($p = 0.52$, Student's *t*-test). (b) There was a significant relationship between the MIC condition and the total serum calcium in females ($p = 0.027$, Student's *t*-test).

Table 4 The results of logistic regression analysis using mandibular inferior cortex (MIC) condition as the dependent variable

MIC condition after 9 years ^a	Odds ratio	Standard error	z	95% CI	p-value
Total serum calcium after 9 years (mg dl ⁻¹)	4.82	2.60	2.91	1.67–13.90	0.004
Sex (0: male, 1: female)	3.26	1.18	3.25	1.60–6.64	0.001
Total serum protein after 9 years (g dl ⁻¹)	0.42	0.18	−2.07	0.18–0.95	0.038
Smoking habit (0: no smoking, 1: previous or current smoker)	1.60	0.34	2.19	1.05–2.44	0.029
Serum phosphorus after 9 years (mg dl ⁻¹)	0.81	0.31	−0.56	0.39–1.70	0.580
Number of subjects					280
Pseudo <i>r</i> ²					0.075

CI, confidence interval.

^a0 indicates no change in MIC classification and 1 indicates change.

a role in declining the speed of bone formation, therefore decreasing the speed of bone resorption by changing the diet and lifestyle are becoming the main options in elderly people. However, despite us finding a relationship, there are no investigations on the relationship between the erosion of the inferior border of the mandible and TSC. The cause of this result in our study is still not clear, and further studies are needed in this area.

Considering that the dynamics of bone formation and bone resorption differ, we suggest it appropriate to define the need for calcium in relation to a specific time or phase of life. In young adults, when the skeleton is mineralized and there is great demand for calcium for bone growth, the calcium requirement will increase as will calcium absorption, resulting in lower TSC.²² In this condition, increasing the calcium intake is one of the crucial factors for maintaining bone formation. On the other hand, in this study TSC increased as a 70-year-old person got older, while the MIC showed greater erosion. These findings suggest that increasing the calcium intake in elderly people did not prevent bone loss. Our results are similar to the other longitudinal studies in which data do not support the hypothesis that dietary calcium intake protects against bone loss.^{12,13}

In this study, means and SDs of hand-grip strength and maximal isometric knee extensor strength significantly differed between subjects whose MIC classification did change and subjects whose MIC classification did not change at baseline and follow-up year (Table 2). Rantanen *et al*²³ said that hand-grip strength correlated with the strength of other muscle groups and is thus a good indicator of overall strength. In old age, decreased muscle strength predisposes people to functional limitations and disability. Brown *et al*²⁴ said that reduced lower maximal isometric knee extensor strength has been associated with a reduction in gait speed, balance, stair-climbing ability and getting up from seated positions. In these groups, early detection and exercise interventions aimed at improving the strength in all muscle groups could potentially lower the risk of subsequent physical disability. Consequently, MIC condition might be used as a sign of decline in physical activity and to advise patients to improve muscle strength by physical exercise at all ages.

Considering the fact that osteoporosis is becoming an increasing health burden worldwide, co-operation between

medical and dental health professionals is necessary to reduce osteoporosis rates. In such cases, dentists can contribute to prevent osteoporosis. Previously, by interpreting single dental panoramic radiographs, we had reported that only females with a Class 3 MIC classification are at high risk for fractures related to osteoporosis.⁶ Whereas, for dentists who have a series of dental panoramic radiographs from a patient, our study found that increased erosion of the inferior border of the mandible is useful for predicting when there is a change in the metabolism of TSC in blood and also only in females. The detection of Class 2 MIC classification in females is becoming more important for preventing further bone loss. Lifestyle and risk factors, such as smoking habits, which decrease bone mineral density should be considered.^{25,26} Moreover, dentists should refer to a medical professional for females with Class 3 MIC classification or with a change into Class 3 MIC classification. Therefore, these findings suggest that dentists should be aware and should further examine females with Class 3 MIC classification to prevent fracture related to bone loss in patients.

Finally, the limitations of this study should be taken into consideration. We found a small positive correlation (pseudo *r*² < 0.1) between MIC condition and TSC levels, but we lacked data about other variables that might influence bone condition, such as vitamin D,^{27,28} magnesium²⁹ and sodium.^{30,31} Although this study on calcium function refers an increased erosion of the inferior border of the mandible as a decline of bodily functions with advancing age,²⁰ we did not precisely measure the calcium intake, absorption and excretion in blood; therefore, the mechanism of elevated TSC still needs to be studied. Furthermore, we did not measure bone metabolism such as bone formation and bone resorption markers. However, it should be noted that the pseudo *r*² in a logistic model cannot be interpreted as *r*² in ordinary least squares, and different pseudo *r*² can arrive at very different values. A pseudo *r*² only has meaning when compared with another pseudo *r*² of the same type, on the same data and predicting the same outcome. In addition, many subjects had dropped out during our 10-year study and had a reduced ability to undergo some measurements on variables that we had measured. As a result, this study ended after 9 years. It will be important to take all those factors into consideration in further studies.

In conclusion, this study suggests that an increase in erosion of the inferior border of the mandible was

significantly associated with elevated TSC after 9 years and only in females.

References

- Klemetti E, Kolmakov S, Kröger H. Pantomography in assessment of the osteoporosis risk group. *Scand J Dent Res* 1994; **102**: 68–72.
- Halling A, Persson GR, Berglund J, Johansson O, Renvert S. Comparison between the Klemetti index and heel DXA BMD measurements in the diagnosis of reduced skeletal bone mineral density in the elderly. *Osteoporosis Int* 2005; **16**: 999–1003. doi: [10.1007/s00198-004-1796-x](https://doi.org/10.1007/s00198-004-1796-x)
- Taguchi A, Tsuda M, Ohtsuka M, Kodama I, Sanada M, Nakamoto T, et al. Use of dental panoramic radiographs in identifying younger postmenopausal women with osteoporosis. *Osteoporosis Int* 2006; **17**: 387–94. doi: [10.1007/s00198-005-2029-7](https://doi.org/10.1007/s00198-005-2029-7)
- Taguchi A, Tanimoto K, Suei Y, Wada T. Tooth loss and mandibular osteopenia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995; **79**: 127–32.
- Taguchi A, Suei Y, Ohtsuka M, Otani K, Tanimoto K, Hollender LG. Relationship between bone mineral density and tooth loss in elderly Japanese women. *Dentomaxillofac Radiol* 1999; **28**: 219–23. doi: [10.1038/sj/dmfr/4600445](https://doi.org/10.1038/sj/dmfr/4600445)
- Kiswanjaya B, Yoshihara A, Deguchi T, Hanada N, Miyazaki H. Relationship between the mandibular inferior cortex and bone stiffness in elderly Japanese people. *Osteoporosis Int* 2010; **21**: 433–8. doi: [10.1007/s00198-009-0996-9](https://doi.org/10.1007/s00198-009-0996-9)
- Deguchi T, Yoshihara A, Hanada N, Miyazaki H. Relationship between mandibular inferior cortex and general bone metabolism in older adults. *Osteoporosis Int* 2007; **19**: 935–40. doi: [10.1007/s00198-007-0526-6](https://doi.org/10.1007/s00198-007-0526-6)
- Blumsohn A, Herrington K, Hannon RA, Shao P, Eyre DR, Eastell R. The effect of calcium supplementation on the circadian rhythm of bone resorption. *J Clin Endocrinol Metab* 1994; **79**: 730–5. doi: [10.1210/jcem.79.3.8077353](https://doi.org/10.1210/jcem.79.3.8077353)
- Andon MB, Smith KT, Bracker M, Sartoris D, Saltman P, Strause L. Spinal bone density and calcium intake in healthy postmenopausal women. *Am J Clin Nutr* 1991; **54**: 927–9.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Long term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial. *Am J Med* 1995; **98**: 331–5. doi: [10.1016/S0002-9343\(99\)80310-6](https://doi.org/10.1016/S0002-9343(99)80310-6)
- Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; **33**: 159–74.
- Van-Beresteijn ECH, Van't-Hof MA, Schaafsma G, De-Waard H, Duursma SA. Habitual dietary calcium intake and cortical bone loss in perimenopausal women: a longitudinal study. *Calcif Tissue Int* 1990; **47**: 338–44.
- Feskanich D, Willett WC, Stampfer MJ, Colditz GA. Milk, dietary calcium and bone fractures in women: a 12-year prospective study. *Am J Public Health* 1997; **87**: 992–7.
- Suleiman S, Nelson M, Li F, Buxton-Thomas M, Moniz C. Effect of calcium intake and physical activity level on bone mass and turnover in healthy, white, postmenopausal women. *Am J Clin Nutr* 1997; **66**: 937–43.
- Ebeling PR, Sandgren ME, DiMaggio EP, Lane AW, DeLuca HF, Riggs BL. Evidence of an age-related decrease in intestinal responsiveness to vitamin D: relationship between serum 1,25-dihydroxyvitamin D₃ and intestinal vitamin D receptor concentrations in normal women. *J Clin Endocrinol Metab* 1992; **75**: 176–82.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R. Influence of age on effects of endogenous 1,25-dihydroxyvitamin D on calcium absorption in normal women. *Calcif Tissue Int* 1994; **55**: 330–4.
- Need AG, Morris HA, Horowitz M, Nordin BEC. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 1993; **58**: 882–5.
- Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. *Kidney Int* 2001; **59**: 2290–8. doi: [10.1046/j.1523-1755.2001.00746.x](https://doi.org/10.1046/j.1523-1755.2001.00746.x)
- Prince RL, Dick I, Devine A, Price RI, Gutteridge DH, Kerr D, et al. The effects of menopause and age on calcitropic hormones: a cross-sectional study of 655 healthy women aged 35 to 90. *J Bone Miner Res* 1995; **10**: 835–42. doi: [10.1002/jbmr.5650100602](https://doi.org/10.1002/jbmr.5650100602)
- Khosla S, Atkinson EJ, Melton JL III, Riggs BL. Effects of age and estrogen status on serum parathyroid hormone levels and biochemical markers of bone turnover in women: a population-based study. *J Clin Endocrinol Metab* 1997; **82**: 1522–7. doi: [10.1210/jcem.82.5.3946](https://doi.org/10.1210/jcem.82.5.3946)
- Davis JW, Ross PD, Johnson NE, Wasnich RD. Estrogen and calcium supplement use among Japanese-American women: effects upon bone loss when used singly and in combination. *Bone* 1995; **17**: 369–73.
- Abrams SA, Griffin IJ, Hawthorne KM, Gunn SK, Gundberg CM, Carpenter TO. Relationships among vitamin D levels, parathyroid hormone and calcium absorption in young adolescents. *J Clin Endocrinol Metab* 2005; **90**: 5576–81. doi: [10.1210/jc.2005-1021](https://doi.org/10.1210/jc.2005-1021)
- Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA* 1999; **281**: 558–60.
- Brown M, Sinacore DR, Host HH. The relationship of strength to function in the older adult. *J Gerontol* 1995; **50**: 55–9.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. *N Engl J Med* 1995; **332**: 767–73. doi: [10.1056/NEJM199503233321202](https://doi.org/10.1056/NEJM199503233321202)
- Kanis JA, Johnell O, Oden A, Johansson H, De Laet C, Eisman JA, et al. Smoking and fracture risk: a meta-analysis. *Osteoporosis Int* 2005; **16**: 155–62.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 1997; **337**: 670–6. doi: [10.1056/NEJM199709043371003](https://doi.org/10.1056/NEJM199709043371003)
- Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, et al. Calcium plus vitamin D supplementation the risk of fractures. *N Engl J Med* 2006; **354**: 669–83. doi: [10.1056/NEJMoa055218](https://doi.org/10.1056/NEJMoa055218)
- Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Takeyama H, Yamada H, et al. Balances of calcium, magnesium and phosphorus in Japanese young adults. *J Nutr Sci Vitaminol* 2004; **50**: 19–25.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 1995; **62**: 740–5.
- Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Matsuzaki N, Takeyama H, et al. Equilibrium intakes of calcium and magnesium within an adequate and limited range of sodium intake in human. *J Nutr Sci Vitaminol* 2006; **52**: 402–6.