Acta Med. Nagasaki 37:158–162

Bone Atrophy after Gastrectomy

Harumi Kida, MD.

The First Department of Surgery, Nagasaki University School of Medicine (Prof. Masao Tomita)

Bone atrophy was assessed in the 500 patients with gastrectomy by using a method of microdensitometry (MD) which was x-rayed on the second metacarpal bone with an aluminum step wedge.

The occurrence of bone atrophy after gastrectomy was apparently significant in females and older patients at age 60 or more.

There was no close correlation with primary disease and postoperative duration. In contrast, the extent of a resection was one of the influential factors on postgastrectomy bone atrophy.

Administration of the activated vitamin D (1α-OH-D_3) was found effective in prevention of the incidence of bone atrophy with advancing age after analysis of the 110 patients with one year adnministraiton of 1α-OH-D_3.

In addition, the effect of calcium is predicted as far as the serum 1.25 $(OH)_2D_3$ levels be obtained. This is one of the important monitors to know the efficacy of calcium given in order to avoid occurring bone atrophy after performing gastrectomy.

Introduction

Bone atrophy after gastrectomy has been surveyed and recognized in Western population. Nevertheless, in Asisan countries, surveys of bone atrophy after gastrectomy has been rarely reported, despite prevalence of gastrectomy for gastric carcinoma and peptic ulcer diseases.

Recently, the technical improvement in bone mineral assay has been far advanced. In addition, patient's life longevity enabled surgeons to investigate bone atrophy after gastrectomy and also to prevent restriction of daily life style with advancing age in association with the development of a new activated-vitamin D preparation for a search for a high quality of the treatment of osteomalacia.

In maintenance of high quality of life after surgery it is necessary to investigate bone marrow abnormality by surgical insult and to know the efficacy of activated vitamin D preparation for bone atrophy.

The purpose of this study is to clarify the degree of bone disorder after gastrectomy as well as to evaluate the efficacy of activated vitamin D preparation.

Materials and Methods

The present study is comprised of 500 patients who underwent a resection of the stomach at the First Department of Surgery, Nagasaki University Hospital and the 15 affiliated hospitals. Males were predominant in a ratio of 2.3:1 with a mean age (years) ± SD of 60.1 ± 10.4 (range 24-88). The primary diseases were gastric cancer in 290 (58.0%), peptic ulcer in 203 (40.6%) and other disorders in 7 (1.4%). The mean interval (years) ± SD from surgery to the survey was 5.6 ± 2.4 (range 0.5-33). The operative procedures used were partial gastrectomy which included 80% or less resection of the stomach in 382 (76.4%), total gastrectomy in 63 (12.6%) and subtotal gastrectomy which composed of a resection of more than 80% of the stomach in 55 (11.0%), respectively.

Bone density was measured by using the microdensitometry (MD) method as described by Inoue et al, [1]which originated from the method of Barnett and Nordin[2] in 1960.

The second metacarpal bone was used for the x-ray scan with an aluminum step-wedge, and the scan density was analysed with a densitometer and a computer. The evaluation of bone atrophy was graded in five categories by scores, that is, normal (score 0-3), initial stage (score 4-6) and degree I (score 7-9), II (score 10-12) and III (score 13-18) as shown in Fig 1. Fig 2 and 3 demonstrate a degree II (score 12) and of the normal (score 0) in the second metacarpal bone on x-Ray films.

Microdensitometry indices were as follows:

D: bone width, d: marrow width, d_1: cortical width on the ulnal side, d_2: cortical width on the radial side. GS max_1: Peak of the cortex on the ulnar side, GS max_2: peak of the cortex on the radial side. GS min: Peak of the middle portion of the bone marrow.

MCI (metacarpal index)=$(d_1+d_2)/D$

GS max=(GS max_1+GS mas_2)/2

Σ GS: a value obtained by computer

integrating the pattern area which is obtained optico-densitometrically and converted into the number of steps

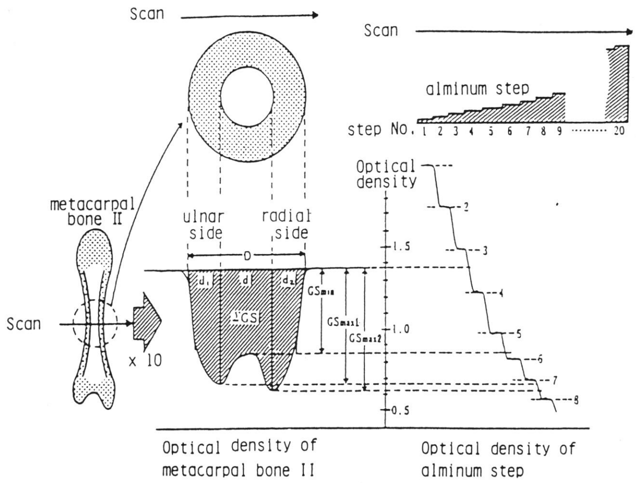

Fig. 1. Method of microdensitometry

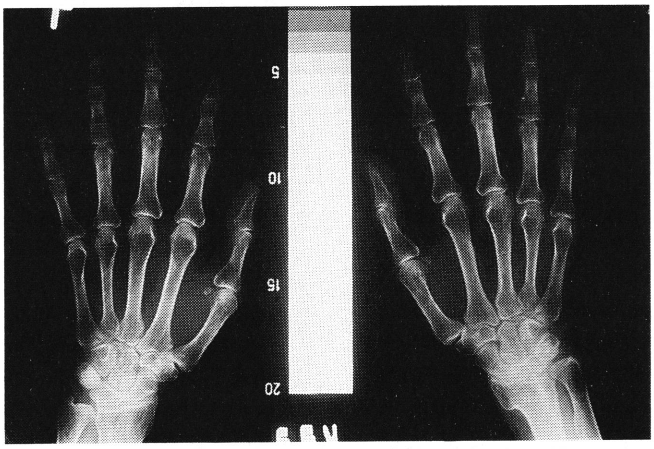

Fig. 2. X-ray of the second metacarpal bone a grade II bone atrophy (score 12)

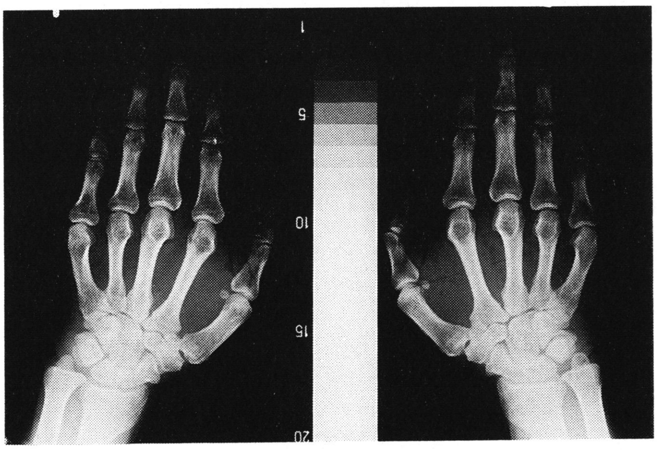

Fig. 3. X-ray of the second metacarpal bone normal pattern (score 0)

on the albuminum step-wedge. The value obtained by dividing Σ GS by bone width D corresponds to the bone mineral content determined by bone mineral analyzer.

In addition, the efficacy of an activated vitamin D, 1α-OH-D_3 was tested on 110 patients with bone atrophy expressed as scores of more than four. Those who were eligible for this study were prescribed with a dosage of 1.0 μg/day of 1α-OH-D_3 for a 1-year period.

Bone atrophy was expressed by scores of more than four. In order to clarify the efficacy of vitamin D, 1α-OH-D_3, changes in scores expressed by densitometery in patients with a resection of the stomach was carefully observed in the follow-up course. In addition, the plasma 1.25 $(OH)_2D_3$ concentration was meaured by Eisman' method. The normal was in a range of 20 pg/ml to 76. Briefly, 1.0 ml of blood sample (serum) was centrifuged at 250 rpm for 10 min, added 1 mol of CH_3CN, centrifuged at 2000 rpm for 10 min at 4 ℃, removed supernatants, added 1.0 mol of CH_3CN, centrifuged at 2000 rpm for 10 min at 4 ℃, resuspended and added 3 ml of 0.4M K_2HPO_4, shaked at 200 rpm for 10 min. Samples were transferred to bond clut (STD Assay Pool) and poured to the receptor in ice, incubated for 2 hours and in 1.25 $(OH)_2D_3$ assay hot at 4 ℃ for 16 hours, added 200 μl of DCC, incubated in ice, centrifuged at 3000 rpm for 10 min at 4 ℃, diluted with 0.6 ml supernant to 7 ml acuazol and counted.

Needless to say, bone atrophy after gastrectomy is influenced by age. Therefore, the results of administering 1α-OH-D_3 were compared according to ages. The sequential observation of comprehensive evaluation in microdensitometry was made in the 13 patients after gastrectomy. For statistical analysis of the data Spearman's and x^2 text were used as determination of statistic significance with $p < 0.05$.

Results

The results of bone densitometry were shown in Table 1 and 2. Males were predominant at a ratio of 2.3:1. According to primary gastric disorders, the main diseases were gastric carcinoma and peptic ulcer. And both were almost equal in number. Partial gastrectomy was mainly applied, and a total and subtotal gastrectomy was performed in one fifth, as shown in Table 1, respectively. With respect to patient's age, the incidence of bone atrophy increased with

Table 1. Patients eligible for this study

	Male	Female	
No	349	151	2.3:1
Primary disorder			
gastric carcinoma		290 (58.0%)	
paptic ulcer		203 (40.6%)	
other disorders		7 (1.4%)	
Operative method			
partial gastrectomy		382 (76.4%)	
total gastrectomy		63 (12.6%)	
subtotal gastrectomy		55 (11.0%)	

advancing age. Female, in particular, is more dominant than male in terms of affection of bone atrophy. In female, bone atrophy is more frequently seen at age 50. In contrast, it was proportional to aging in male as shown in Table 2.

Table 2. Results of bone densitometry

Male 349	result of densitometry by ages				
	normal	initial stage	Degree of I	Degree of II	Degree of III
age					
~39	12	4	0	0	0
40~	32	2	1	2	0
50~	86	16	7	4	0
60~	54	14	10	5	7
70~	41	14	12	5	8
80~	2	5	1	1	4
Female 151					
~39	2	1	2	0	0
40~	13	3	1	0	0
50~	23	14	10	2	6
60~	9	11	7	7	4
70~	9	8	9	3	1
80~	0	4	2	0	0

Table 3 shows the difference in the occurrence of bone atrophy between male and female. It is characteristic of a high incidence of bone atrophy in female, in particular, at age 50 or more. However, the degrees of bone atrophy were not so severe as to become degree III with age.

Table 3. Incidence of bone atrophy by sex distribution

		result of densitometry				
		normal	initial	Degree of I	Degree of II	Degree of III
All patients	500	283	96	62	29	30
Male	349	227	55	31	17	19
Female	151	56	41	31	12	11

Table 4 shows the influential factors on bone atrophy after gastrectomy. It is indicated that female was characteristic of the predominant factor. Nevertheless, there was no significant correlation. And also there was no correlation with primary diseases regardless benign and/or malignant diseases. The postoperative duration was not responsible for occurrece of bone atrophy. A subtotal or total gastrectomy showed a significant trend to be liable to bone atrophy in long follow-up period, particularly in female at age 50 or more. Furthermore, the reconstructive method after gastrectomy did not relate to bone atrophy, indicating almost a similar incidence of bone atrophy no matter how operative method may apply for reconstruction. Bone atrophy after the reconstruction by Roux-en Y and interposition seemed to be slightly high in reflection of inclusion of total gastrectomy as shown in Table 5.

Table 4. Summary of incidence of bone atrophy after gastrectomy

	total	bone atrophy	
Sex			
Male	349	122	34.9%
Female	151	95	62.9
Primary diseases			
Gastric carcinoma	290	141	48.6
Peptic ulcer	203	75	36.9
Other disorders	7	1	14.3
Postoperative duration			
~1.9	10	5	50.0
2.0~4.9	279	129	46.2
5.0~8.9	163	67	41.1
9.0~	48	16	33.3
Operative procedures			
partial gastrectomy	382	146	38.2
total gastrectomy	63	33	52.4
subtotal gastrectomy	55	38	69.1

Table 5. Reconstruction method

	total	atrophy	%
Billroth I	354	154	43.5
Billroth II	80	28	35.0
Roux-enY	50	26	52.0
Interpotision	16	9	56.2

The benefit of vitamin D_3, 1α-OH-D_3 was evaluated on the 110 patients with resection of the stomach in prevention of bone atrophy caused by gastrectomy.

As shown in Table 6, for a total of 110 patients 1α-OH-D_3 were prescribed during a 1-year period after gasterctomy. Forty-five percent of all patients revealed improvement and eighteen percent had no change, indicating the same scores as the values of preadministraiton. As compared with non-treated group with 1α-OH-D_3, it is apparent that bone atrophy had benefits from vitamin D_3 administration following a resection of the stomach. The incidence of bone atrophy with advancing age was reduced in comparison with the tendency toward natural aging change.

This beneficial tendency of this drug was observed in at

Table 6. Preventive effect of 1α-OH-D_3 prescribed on bone atrophy induced by gastrectomy

Period of 1α-OH-D_3 administration	Changes in scores by densitometry					
12 months age distribution	total	improved (decrease)		no change	deteriorate (increase)	
~39	6	5	83.3%	1	0	
40~	13	10	76.9%	3	0	
50~	23	13	56.5%	3	7	30.4%
60~	32	14	43.7%	5	13	40.6%
70~	30	8	26.7%	6	16	53.3%
80~	6	0		3	3	50.0%
total	110	50	(45.4%)	20 (18.2%)	39	(35.4%)

least three months after administration of 1α-OH-D_3. It was implicated that determination of the benefical effect of the drugs in prevention of bone atrophy required approximately six months after initiation of the drug administration.

The drug enabled older patients to prevent a trend to deterioration although it failed to obtain improvement. Fig. 4 revealed the result of comprehensive evaluation of microdensitometry in the 13 patients after gastrectomy. And also, changes in the serum 1.25 $(OH)_2D_3$ levels were observed in 10 patients to assess the progress in bone atrophy after gastrectomy. Fig. 5 revealed an increase in the 1.25 $(OH)_2D_3$ levels in the serum in 9 months or more after gastrectomy in reflection of the progression of bone atrophy.

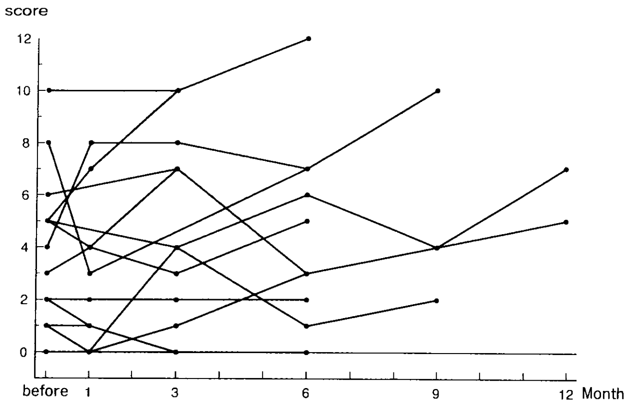

Fig. 4. Sequent observation after gastrectomy on the scores by microdensitometry

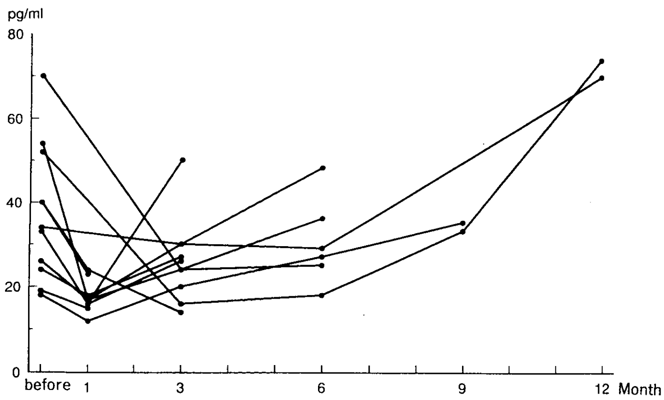

Fig. 5. Changes in the 1.25-$(OH)_2D_3$ levels in the serum after gastrectomy

Discussion

Recent studies were focused on bone atrophy after gastrectomy reflecting the desire for a good quality of life after gastrectomy.

Deller[3] clarifed that thirty to ninety-five percent of the patients with gastrectomy had revealed a finding of osteomalacia. Whereas, it has been accepted in Europe[4] that a common cause of osteomalacia is postgastrectomy bone abnormality. So far, a wide range of the incidence of bone atrophy after gastrectomy had been reported, ranging from one to 30 percent in incidence. It is due to the difference in patient's age and sex distribution, the modality of the operative procedure and the examination method used for bone atrophy in the different bones.[5-8]

In Japan, there was a report of five percent of the incidence after gastrectomy in 1971.[9] In contrast, recent reports[10-13] show higher incidence of 52 to 71% in incidence of bone atrophy. It is based on more improved diagnostic modalities which make it possible to detect a minimal bone abnormality in asymptomatic patients. Needless to say, such a subclinical asymptomatic patient with bone mineral content is warned to be susceptible to fracture even by blunt trauma, and to increase a risk of developing fracture.

In this series, it is defined that the incidence of bone atrophy is not significantly related to the follow-up duration after surgery. It is shown that the appearance of bone atrophy is notably high in female and in the age over 70 years.

Hirota et al[11] reported the incidences of osteomalacia and osteoporosis after gastrectomy, identifying bone atropohy from osteomalacia and osteoporosis by the biopsy specimen obtained from the 11th rib. They certified that the incidences of osteomalacia are as high as 0.8% after partial gastrectomy and 7.7% after total gastrectomy and also those of osteoporosis are 59% following partial and 76% following total gastrectomy.

It is well known that biochemical changes occure in high serum alcaline phosphatase, low serum calcium and organic phosphate. In particular, the high value of alcaline phosphatase in the serum is indispensable for the diagnosis of bone atrophy to be precisely determined. As reported by Koyama,[13] osteomalacia is suggested by the biochemical findings of low values of serum calcium and phosphate with an increase in alcaline phosphatase.

It is true without saying that osteomalacia should be named by x-ray finding. It is no doubt that the severity of bone atrophy after gastrectomy is directly influenced by patient's age and sex, dietary intake of calcium, and daily life style of exposure to sunlight.

A decrease in the secretion of gastric acid after gastrectomy is one of the major causes of calcium malabsorption.[15] It is recommended that daily intake of warm milk is of great value to prevent bone atrophy after gastrectomy. In a postmenopausal osteoporotic patient daily intake of calcium as many as 1500 mg is needed.[16] Inadequate exposure to sunlight is a promoting factor of bone atrophy. Prescription of vitamin D_3 is mandatory for the prevention or the treatment of bone atrophy in such a patient. And also it is well known that osteomalacia is attributable to postoperative steatorrhoea which may be associated with the operative procedure of Billroth II gastrectomy causing obstruction in the duodenum.[14]

Densitometric data clarified that 1α-OH-D_3 increases bone density which implies a promoting action of mineral accumulation in the bone. It, however, did not make the bone cortex widened.

It is recommended that the combination of calcium plus activated vitamn D is required for the treatment of bone atrophy after gastrectomy. In this study, the administration of activated vitamin D is of great help to minimize degenerative bone changes in response to advancing age.

Ozawa et al[16] reported that the final metabolite of vitamin D was 1.25 $(OH)_2D_3$ which increased after gastrectomy. In contrast, the serum 25-OH-D_3 levels were reduced. They pointed out that, despite a shortage of the storage of vitamin D in the body. Vitamin D was activated and the state of the secondary hyperparathyroidism was provoked.

The causes of bone atrophy after gastrectomy are concerned in the genesis of 1) reduced food intake, 2) decrease in secretion of gastric acid, 3) increase in insoluble calcium due to stearrhea 4) malabsorption of calcium from the gut. In consequence, hypocalcemia is provoked, next the state of secondary parathyroidism may be introduced. Consequently absorption of calcium and fat-soluble Vitamin D may be diminished. On the other hand, Vitamin D_3 is changed into 25-OHD_3 in the liver and into 24.25 $(OH)_2D_3$ and 1.25 $(OH)_2D_3$ in the kidney by hydroxy enzyme. On the other hand, in proportion to serum calcium decrease 25-OHD_3 is actively changed into 1.25 $(OH)_2D_3$ in the kidney with the help of PTH which is secondly increased. As a result, the level of 1.25 $(OH)_2D_3$ is elevated. In this series, the levels of 1.25 $(OH)_2D_3$ in the 10 patients were followed in the postoperative course of gastrectomy. The serum 1.25 $(OH)_2D_3$ levels were gradually increased with the elapse of 9 months or more. It is in response to maintaining the normal level of the serum calcium by the action of activated 1.25 $(OH)_2D_3$ in the kidney with an aid of the PTH function. These results imply that an increase in the 1.25 $(OH)_2D_3$ levels compensates the reduced plasma calcium level for the normal.

Needless to say, it is known that the duodenum and the upper jejunum have a key role in absorption of calcium. And also the intraluminal pH level is greatly influential on absorption of calcium from the gut. Miyao[17] clarified that the amount of calcium absorbed at pH 9 is appriximately half of those at pH 4. It is assumed that calcium absorption from the gut is, in part, affected by the intraluminal pH. Since the output of gastric acid after gastrectomy is significantly reduced, absorption of calcium may well diminish. An increase in the plasma 1.25 $(OH)_2D_3$ levels is a symbol of compensation for impaired calcium absorption after gastrectomy.

As far as an increased 1.25 $(OH)_2D_3$ level may be obtained, it is in response to the maintenance of the serum calcium level. During the period of observation of high serum 1.25 $(OH)_2D_3$ levels in the postoperative foollow-up patients with gastrectomy, it is suggested that 1α-OH-D_3 administration in combination with calcium should be required and their effects should be expected.

Recently Eastwood et al[18] reported that a decrease in the serum 25-OH-D_3 and 24.25-$(OH)_2D_3$ levels was obtained in patients with undernutritional osteomalacia, although the serum 1.25 $(OH)_2D_3$ levels had been kept almost normal. Thompson[4] also reported that Vitamin D absorption in patients with partial gastrectomy was impaired without exception. However, they clarified that impaired absorption of Vitamin D were not severe but remaines slight.

Further study should be accumulated to clarify the mechanism in the genesis of bone atrophy after gasterectomy and to find out a better preventive procedure from metabolic bone disease after gastrectomy.

References

1) Inoue T, Kushida K, Yamashita G: Radiological assesment of bone density using microclensitometer (in Japanese) Kotutaischya 14:91-104, 1981.
2) Barnett E, and Nordin BEC: The radiological diagnosis of osteoporosis: A new approach. Clin. Radiol. 11:166-174, 1960.
3) Deller DJ, Edwards RG, Addison M: Calcium metabolism and the bones after partial gastrectomy II. The nature and cause of the bone disorder. Aust Ann Med 12:295-309, 1963.
4) Thompson GR, Lewis B, Booth CC: Vitamin-D absorption after partial gastrectomy. Lancet 1:457-458, 1966.
5) Morgan DB, Pulvertaft CN: Effects of vagotomy on bone metabolism. In: Williams JA, Cox AG eds. After vagotomy. London: Butterworths 1969:167-171
6) Williams JA: Effects of upper gastro-intestinal surgery on blood formation and bone metabolism. Br J Surg 51:125-135, 1964.
7) Clark CG: Disordered calcium metabolism after polya partial gastrectomy. Lancet 1:734-738, 1964.
8) Eddy RL: Metabolic bone disease after gastrectomy. Am J Med 50:442-449, 1971.
9) Niwayama M; Bone disease following gastrectomy. Nippon Geka Gakkai Zasshi 72:549-573, 1971.
10) Fukuda M, Shibata H, Hatakeyama K et al: Difference in calcium metabolism following Billroth-I and Billroth-II procedures for gastric and duodenal ulcers. Jpn J surg 9:295-303, 1979.
11) Hirota M: A clinical and histological evaluation of bone diseases following total gastrectomy (in Japanese). Nippon shokakigeka Gakkai Zasshi 15:1716-1727, 1982.
12) Nishimura O, Sakamoto H, Furumoto T et al: Bone disorder in long-term survival after gastrectomy with referrence to bone mineral content (in Japanese with English abstract). Nippon geka Gakkai Zasshi 88:1684-1694, 1987.
13) Koyama M, Muto T, Hirota M et al: Postgastrectomy bone disease (in Japanese). Shokaki geka 3:1701-1709, 1980.
14) Fukuda M, Hirota M, Sato S: Bone lesions and dental caries after gastrectomy-Evaluation of milk intolerance and operative procedure. Jpn J Surg 16:36-41, 1986.
15) Baylink DJ: Bone volume regulation and osteoporosis bone resorption, bone formation and coupling factor. In Itami Y, Inoue T, Orimo H eds. Advances in research of osteoporosis Tokyo: Life science Public Inc 25-85, 1984.
16) Ozawa K, Shimazu H, Kobori O et al: Vitamin D and calcium metalolism after gastrectomy-parathyroid function and bone chages (in Japanese), Jpn. J. Gastroenterol. 19:205, 1986.
17) Miyao M: Intestinal absorption of calcium. Ped. Clin. 18:961-970, 1965.
18) Eastwood JB, de Wardener HE, Gray RW: et al: Normal plasma 1.25 $(OH)_2$-Vitamin D concentrations in nutritional Osteomalacia. Lancet 1377-1378, 1979.