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Changes in Volumetric Bone Mineral Density After Gastrectomy as Assessed by Dual Energy X-ray Absorptiometry

Kiyotaka Yabuki[1], Koichi Sato[1], Takeo Maekawa[1], Hidenori Tsumura[2] and Yozo Watanabe[2]

[1] Department of Surgery, Juntendo Izunagaoka Hospital, Juntendo University School of Medicine
[2] Department of Surgery, Koshigaya Municipal Hospital

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Abstract

We used dual energy X-ray absorptiometry (DXA) to study changes in estimated volumetric bone mineral density (EstVBMD) of the lumbar spine after gastrectomy. The study group comprised 41 men and 32 women. When EstVBMD was compared according to sex among patients younger than 60 years of age, patients 60 to 69 years of age, and patients these three groups in men (0.185 g/cm^3, 0.187 g/cm^3, 0.187 g/cm^3, respectively). In contrast, EstVBMD was significantly lower in women 60 to 69 years of age (0.157 g/cm^3) and those 70 years of age or older (0.159 g/cm^3) than in women younger than 60 years (0.200 g/cm^3) ($P<0.01$). When the relation between EstVBMD and the number of months after gastrectomy was studied according to sex in patients younger than 70 years, EstVBMD negatively correlated with the interval after operation in men ($r=-0.365$, $P<0.05$), whereas there was no correlation between these variables in women. These results suggest that after gastrectomy bone mineral density decreases gradually in men younger than 70 years, but not in women. The lack of a consistent change in bone mineral density after gastrectomy in women is apparently caused by the marked effect on bone metabolism of decreased female hormone levels after menopause.

Introduction

Gastrectomy is often performed in the field of gastroenterological surgery. This procedure is associated with various types of functional and organic sequelae. Functional impairment includes conditions such as dumping syndrome, malnutrition, lactose intolerance, and diarrhea. Organic disturbances include reflux esophagitis, afferent loop syndrome, and disturbed bone metabolism. Among these sequelae, disturbed bone metabolism after gastrectomy has recently received attention because of the increasing numbers of long-term survivors after gastrectomy for gastric carcinoma.

Many problems have interfered with attempts to study the effects of gastrectomy on bone. A

Present address: Kiyotaka Yabuki, 1129 Nagaoka, Izunagaoka-cho, Tagatagun, Shizuoka 410–2211, Japan
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major limitation was lack of techniques to accurately measure bone mineral density. Recently, however, several quantitative techniques have been developed, such as microdesitometry (MD), single energy X-ray absorptiometry, dual energy X-ray absorptiometry (DXA), quantitative computed tomography (QCT), and ultrasound bone densitometry. Before the development of these techniques, no method could reproducibly estimate bone mineral density. Consequently, early changes were not detected, and bone disturbances were already relatively advanced at the time of detection (1, 2, 3), or such disturbances were reported to occur in 6.5% to 44.4% of patients who undergo gastrectomy (4, 5, 6, 7, 8). Another reason precluding studies of changes in bone metabolism was the complex relation with demographic factors. As for age, it is very difficult to distinguish age-related changes from the effects of gastrectomy. This problem is compounded in perimenopausal women who undergo gastrectomy, in whom the effects of the procedure on bone mineral density remain largely unknown and may be masked by the influence of estrogen deficiency.

To improve our understanding of the effects of gastrectomy on bone metabolism, we used DXA, a new, very accurate and reproducible technique that exposes the patient to a minimal dose of radiation (9, 10, 11), to estimate volumetric bone mineral density (EstVBMD) of the lumbar spine after gastrectomy. Changes in bone mineral density after the procedure were study according to age and sex.

Patients and Methods

Bone mineral density was estimated by DXA in 73 patients (41 men and 32 women) who underwent gastrectomy at the Department of Surgery, Juntendo Izunagaoka Hospital, Juntendo University School of Medicine between 1991 and 1996. Patients were excluded if they had concurrent diseases affecting bone metabolism or extreme deformity of the lumbar spine, or if they were receiving steriods, vitamin D, or calcium preparations. Mean age at the time of measuring bone marrow density was 64.0±8.46 years (range, 45 to 80). Twenty patients (8 men and 12 women) were younger than 60 years, 33 (23 men and 10 women) between 60 and 69 years of age, and 20 (10 men and 10 women) 70 years of age or older. Eight patients (5 men and 3 women) had peptic ulcer, and 65 had gastric carcinoma (36 men and 29 women). The operative procedure involved total gastrectomy with Roux-en-Y anastomosis in 15 patients (11 men and 4 women), distal gastrectomy with Billroth's I Reconstruction in 57 patients (29 men and 28 women), and Billroth's II Reconstruction in 1 patient (1 man). All patients with gastric carcinoma underwent radical operation, and there was no recurrence. The interval from surgery until the time of measuring bone mineral density ranged from 12 to 158 months (mean 58.3±38.9 months).

DXA was performed with the use of a Hologic (Waltham, Maryland, USA) model QDR-2000 bone densitometer. The bone mineral density of the 2nd through 4th lumbar vertebrae was measured in an anteroposterior direction (AP) and in a lateral direction (Lat), with the patient in supine position. The estimated volumetric bone mineral density (EstVBMD) was assessed by dividing the bone mineral content in a lateral plane by the vertebral volume. The vertebral volume was calculated by the following formula; vertebral volume=vertebral area in a lateral plane×width in an anteroposterior plane. The data were analyzed with using the Student's t-test and Pearson's correlation coefficient. Differences with a P value less than 0.05 were considered statistically significant.

Results

Among all subjects, there was a significant positive correlation between AP and EstVBMD ($r=0.756$, $P<0.01$) (Fig. 1). Bone marrow density of the lumbar vertebrae was compared between men and women after gastrectomy. Mean age at the time of examination was 64.9 ± 6.69 years in men and 62.8 ± 10.3 years in women. Mean AP was 0.901 ± 0.153 g/cm^2 in men and 0.767 ± 0.187 g/cm^2 in women. Mean EstVBMD was 0.187 ± 0.026 g/cm^3 in men and 0.174 ± 0.033 g/cm^3 in women. There was no difference between men and women in either AP or EstVBMD (Fig. 2). Bone mineral density in each sex was then compared according to the operation procedure. In men, AP was 0.894 ± 0.172 g/cm^2 after distal gastrectomy and 0.919 ± 0.108 g/cm^2 after total gastrectomy; EstVBMD was 0.186 ± 0.029 g/cm^3 after distal gastrectomy and 0.186 ± 0.018 g/cm^3 after total gastrectomy. None of these differences were significant (Fig. 3-A). In women, AP was 0.766 ± 0.184 g/cm^2 after distal gastrectomy and 0.771 ± 0.235 g/cm^2 after total gastrectomy; EstVBMD was 0.175 ± 0.033 g/cm^3 after distal gastrectomy and 0.167 ± 0.042 g/cm^3 after total gastrectomy. These differences were also not significant (Fig. 3-B). Bone marrow density in each sex was then compared according to age at the time of examination. AP was 0.862 ± 0.110 g/cm^2 in men younger than 60 years, 0.914 ± 0.178 g/cm^2 in those aged 60 to 69 years,

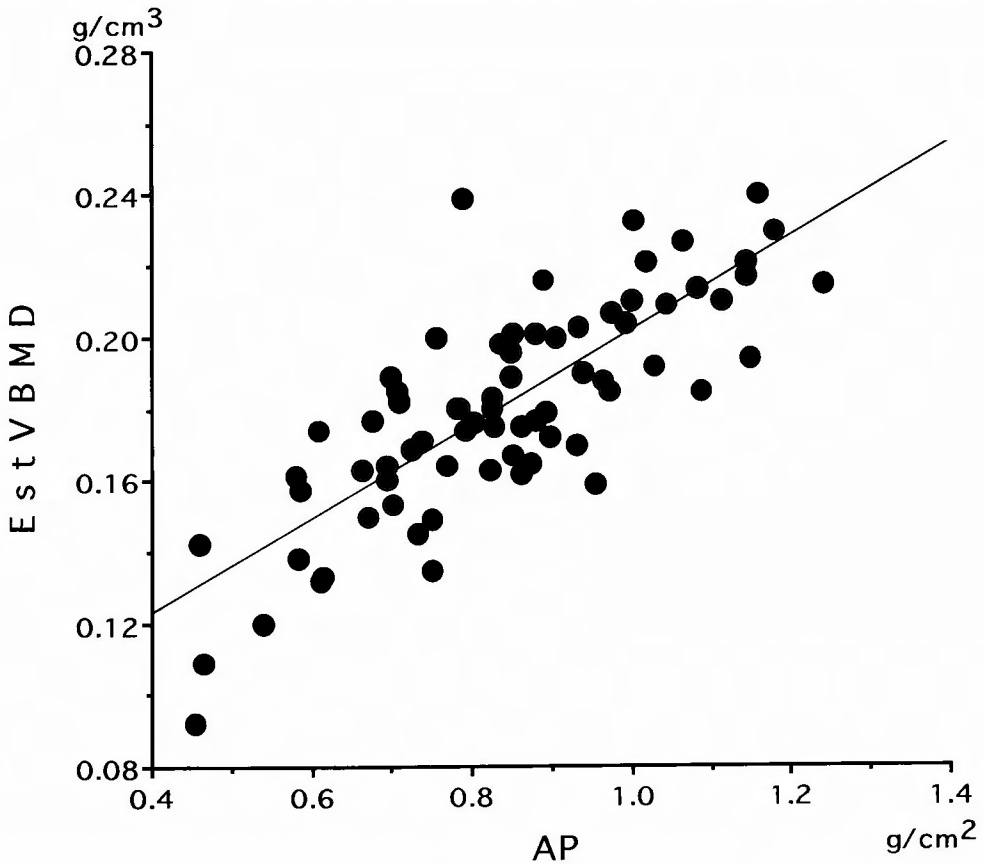

Fig. 1 Relation between AP and EstVBMD in 73 patients undergoing gastrectomy. There was a significant positive correlation between these variables ($y=0.132x+0.0699$, $r=0.796$, $P<0.01$).

and 0.900±0.128 g/cm^2 in those aged 70 years or older. Bone marrow density in men aged 70 years or older and those aged 60 to 69 years did not differ significantly from that in men younger than 60 years. EstVBMD was 0.185±0.022 g/cm^3 in men younger than 60 years, 0.187±0.0285 g/cm^3 in those aged 60 to 69 years, and 0.187±0.027 g/cm^3 in those aged 70 years or older. There was no significant difference in EstVBMD among men younger than men aged 60 to 69 years, those 70 years or older, and those younger than 60 years (Fig. 4-A). In women, AP was 0.877±0.139 g/cm^2 in patients younger than 60 years, 0.698±0.122 g/cm^2 in those aged 60 to 69 years, and 0.703±0.235 g/cm^2 in those 70 years or older. AP was significantly lower in women 60 to 69 years of age and women 70 years or older than in those younger than 60 years. EstVBMD was 0.200±0.23 g/cm^3 in women younger than 60 years, 0.157±0.025 g/cm^3 in those 60 to 69 years, and 0.159±0.032 g/cm^3 in those 70 years or older. EstVBMD was significantly lower in women 60 to 69 years and those 70 years or older than in women younger than 60 years (Fig. 4-B). The relation between bone mineral

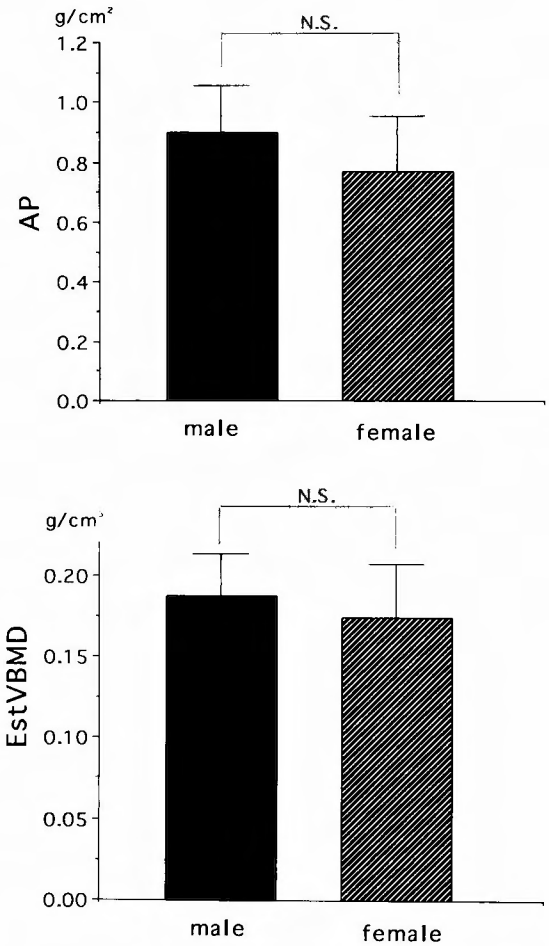

Fig. 2 Comparison of bone mineral density between men and women. Mean AP was 0.901±0.153 g/cm^2 in men and 0.767±0.187 g/cm^2 in women. Mean EstVBMD was 0.187±0.026 g/cm^3 in men and 0.174±0.033 g/cm^3 in women. There was no significant difference between men and women. Values are expressed as means±SD. N.S., not significant.

density and the interval after gastrectomy was studied according to sex among patients younger than 70 years. In men, there was no significant correlation between AP and the number of months after gastrectomy, ranging from 12 to 122 months ($r=-0.253$). However, there was a significant negative correlation between EstVBMD and the number of months after gastrectomy ($r=-0.365$, $P<0.05$) (Fig. 5-A). In women, there was no correlation between AP and the number of months after gastrectomy, ranging from 12 to 151 months ($r=0.0316$); similar results were obtained for EstVBMD ($r=0.158$) (Fig. 5-B). Relation of the interval after surgery to AP and EstVBMD in men younger than 70 years and those 70 years of age or older at the time of operation was studied. In men younger than 70 years, there was no significant correlation between AP and the number of months after surgery ($r=-0.223$). A significant negative correlation was found between EstVBMD and the number of months ($r=-0.365$, $P<0.05$) (Fig. 6-A). In men 70 years of age or older, there was no correlation between AP and the number of months after gastrectomy ($r=-0.0548$); similar results were obtained for EstVBMD ($r=-0.130$) (Fig. 6-B).

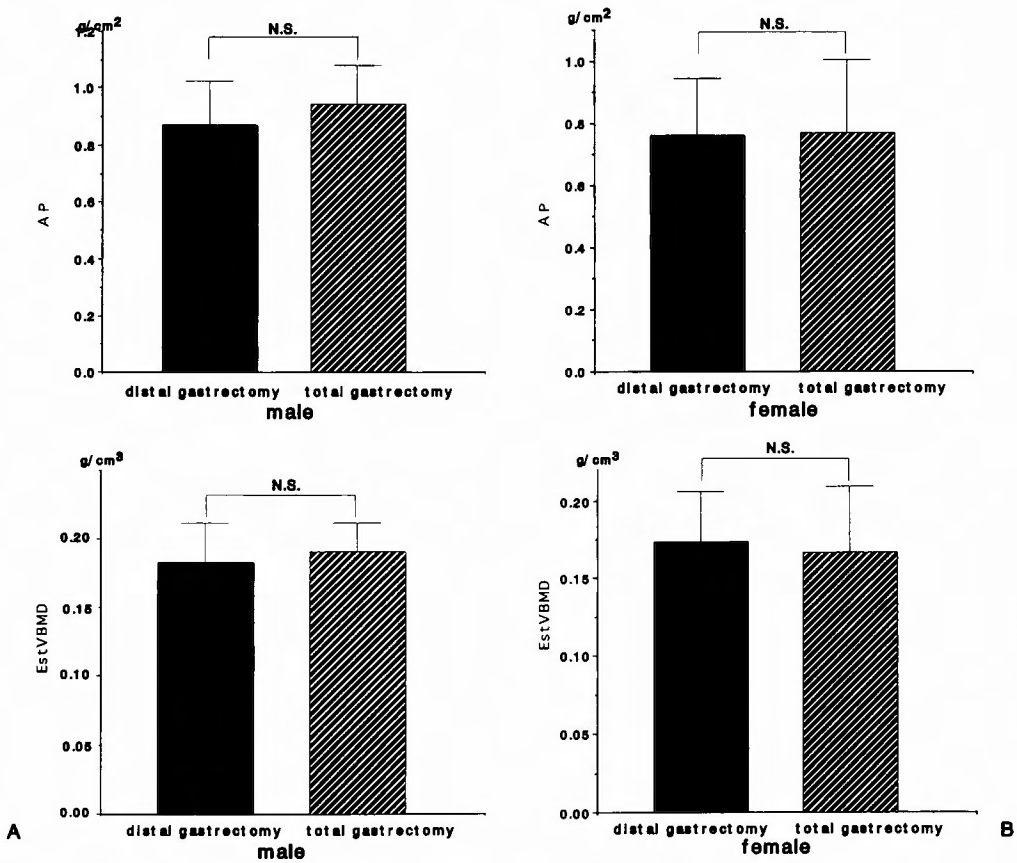

Fig. 3-A and B Bone mineral density according to operation procedure in men and women. In men there was no significant difference in bone mineral density in terms of AP or EstVBMD between patients undergoing distal gastrectomy and those undergoing total gastrectomy (A). In women, there was also no significant difference in either AP or EstVBMD between patients undergoing distal gastrectomy and those undergoing total gastrectomy (B). Values are expressed as means±SD. N.S., not significant.

Discussion

Osteopathy in patients who had undergone gastrectomy was first reported by Sarasin in 1941 (1). Similar reports were made by Pyrah (2) and Baird (3). Subsequent studies reported that patients who undergo gastrectomy have an increased incidence of morbid fractures (7, 12), and osteopathy is now considered not uncommon after gastrectomy. Osteopathy is attributed primarily to disturbed calcium metabolism (4, 7, 13, 14) and impaired absorption of vitamin D (14, 15, 16). The potential roles of lactose intolerance (13, 17) and hyperparathyroidism (17) have also been proposed. The incidence of osteopathy differs depending on the method used to evaluate bone metabolism. Eddy (7) reported an incidence of 24.4% based on simple radiographs of bone. In studies based on bone biopsy, Garrick et al. (6) reported an incidence of 44.4% and Tovey et al. (8) an incidence of 6.5%. In studies using MD, Sugiyama et al. (18) found an incidence of 38%, Tanaka et al. (19) an incidence of 39.8%, and Hirano et al. (20) an incidence of 35%. Havald et al. (4) estimated that osteopathy occurred after gastrectomy at rate of 42.1% on the basis of calcium infusion tests, and John (5) reported an incidence of 19% based on the elevation of serum alkaline phosphatase activity.

We used DXA to measure bone mineral density of the lumbar spine and to study changes in bone mineral content after gastrectomy. DXA has many advantages over conventional techniques, including good image quality, high reproducibility, minimal scanning time, and exposure to a low

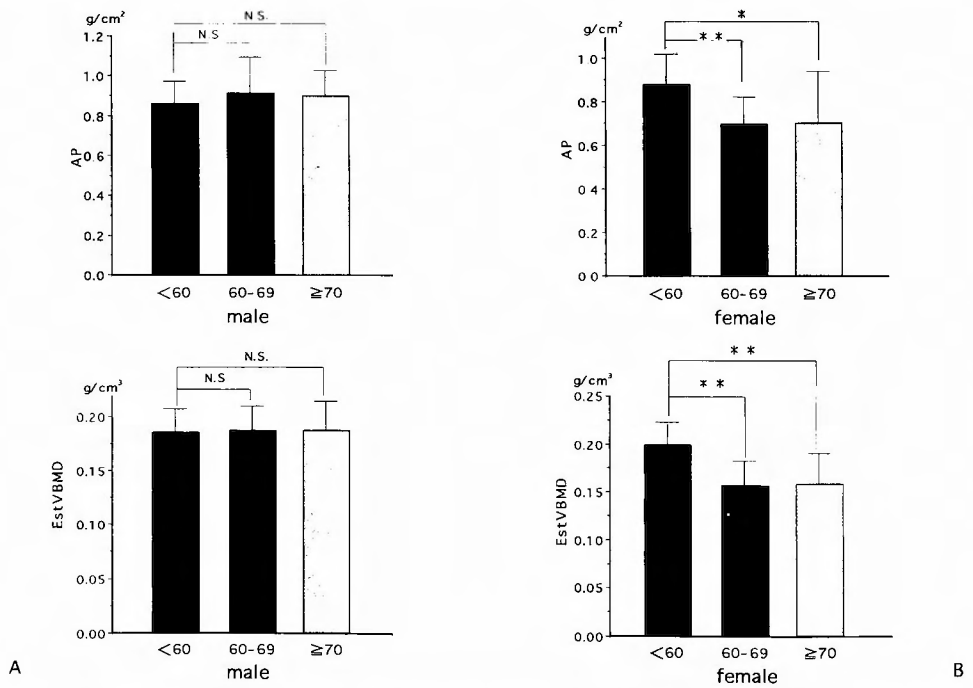

Fig. 4-A and B Bone mineral density according to age in men and women. In men, there was no appreciable difference in either AP or EstVBMD between patients 60 to 69 years of age and those 70 years of age or older (A). In women, both AP and EstVBMD were significantly lower in patients aged 60 to 69 years and those aged 70 years or older than in patients younger than 60 years (B). *P<0.05, **P<0.01. Values are expressed as means±SD. N.S., not significant.

dose of radiation (9). It is an accurate and reliable technique for measuring bone mineral density (10, 11). To accurately estimate bone mineral density of the lumbar spine in the present study, EstVBMD was calculated based on Lat. In previous studies, AP was overestimated because of the effects of age-related changes, such as osteoarthritis and aortic calcification (21). In contrast, Lat eliminates the influence of posterior components and is thus a more accurate measure of the bone mineral density of vertebrae, consisting primarily of cancellous bone with a high rate of metabolic turnover, and is more accurate and effective than other procedures for the detection of osteopenia (22, 23, 24). Instruments that can determine Lat with the subject in a supine position have recently been developed, contributing to improved usefulness (25). EstVBMD, calculated based on Lat, has received considerable attention because it incorporates body build as a factor (25). Sabin et al. (26) studied the relation between the EstVBMD and the actual ash content of the lumbar spine of cadavers and obtained a high correlation coefficient ($r=0.998$), demonstrating that EstVBMD is a reliable measure of actual bone mineral content.

Several studies have assessed the relation between operation procedure and the occurrence of osteopathy. On the basis of simple radiographs of the lumbar spine, Koga et al. (27) reported that the incidence of osteopathy was higher in men who underwent distal gastrectomy with Billroth's II

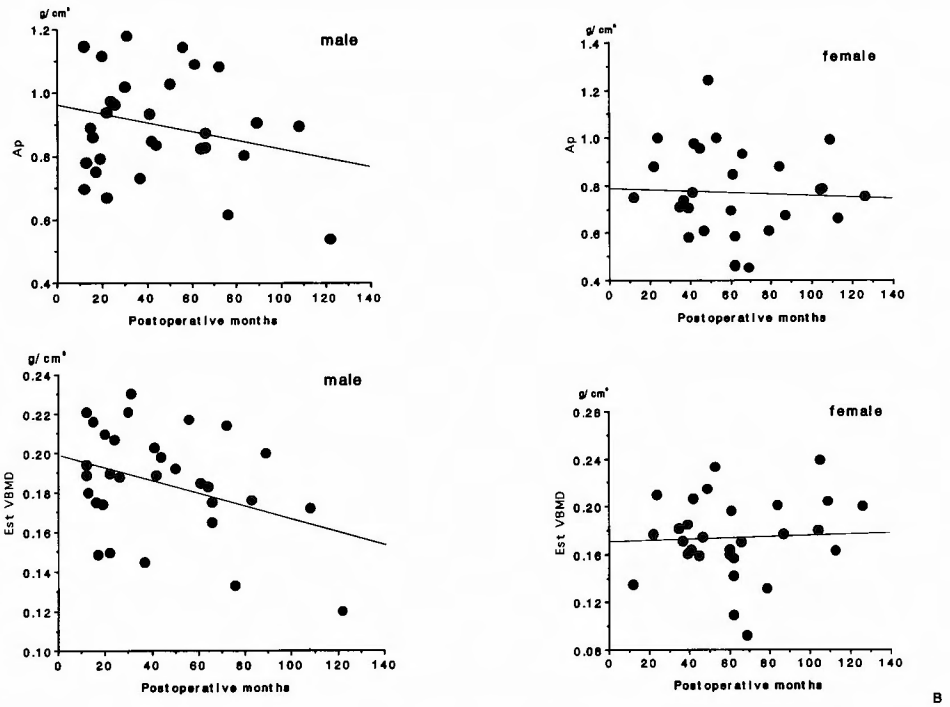

Fig. 5-A and B Relation of the interval after surgery to AP and EstVBMD in men younger than 70 years. There was no significant correlation between AP and the number of months after surgery ($n=31$, $y=-0.00140x+0.962$, $r=-0.253$, N.S.). A significant negative correlation was found between EstVBMD and the number of months after surgery ($n=31$, $y=-0.000325x+0.200$, $r=-0.365$, $P<0.05$) (A). Relation of interval after surgery to AP and EstVBMD in women younger than 70 years. AP and the number of months after surgery were independent variables ($n=22$, $r=0.0316$, N.S.); similar results were obtained for EstVBMD ($n=22$, $r=-0.158$, N.S.) (B). N.S., not significant.

Reconstruction or total gastrectomy than in those who underwent distal gastrectomy with Billroth's I Reconstruction. On MD analysis, Sugiyama et al. (18) found that the incidence of osteopathy was significantly higher in patients who received total gastrectomy (42.2%) than in those who received distal gastrectomy (38.8%). Tanaka et al. (19) reported the highest incidence of osteopathy after total gastrectomy (51.6%), followed by distal gastrectomy with Billroth's I Reconstruction (37.2%) and distal gastrectomy with Billroth's II Reconstruction (23.3%). Hirano et al. (20) found that the incidence of osteopathy after partial gastrectomy (28.5%) was significantly lower than that after subtotal gastrectomy (68.8%) or total gastrectomy (48.3%). In contrast, Inoue et al. (28) found no significant difference in bone mineral density as determined by DXA between patients who underwent total gastrectomy and those who underwent distal gastrectomy with either Billroth's I or Billroth's II Reconstruction. Nihei et al. (29) determined the bone mineral density index by QCT and found no significant difference between patients after distal gastrectomy and those after total gastrectomy. Our study also showed no difference in bone mineral density between patients undergoing distal gastrectomy and those undergoing total gastrectomy.

As for the relation between the interval after surgery and the occurrence of osteopathy, Koga et al. (27) reported no difference in the incidence of osteopathy between 5 to 10 years after operation

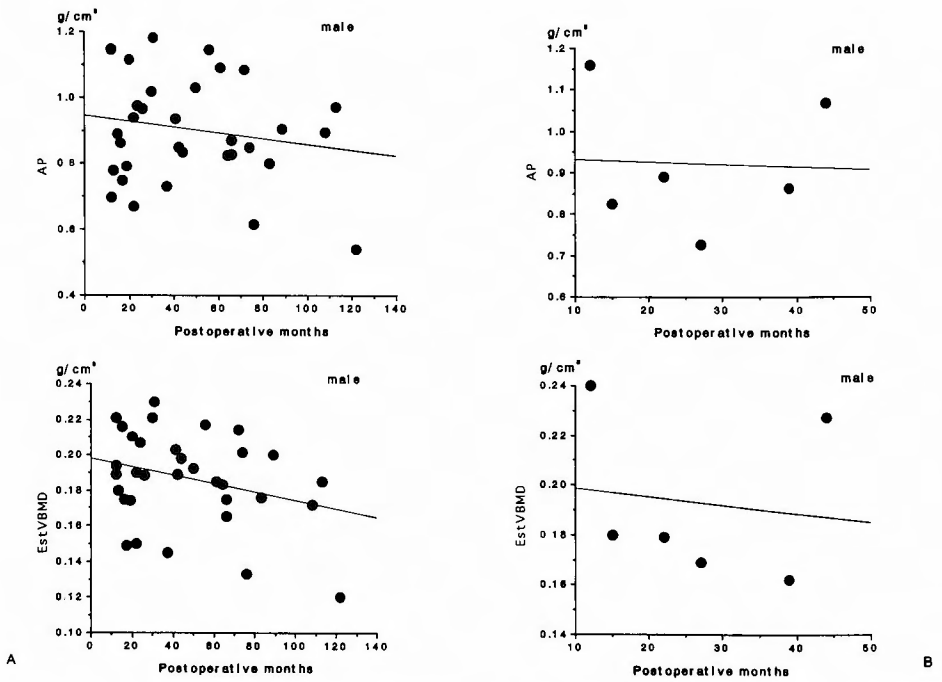

Fig. 6-A and B Relation of the interval after surgery to AP and EstVBMD in men younger than 70 years and those 70 years of age or older at the time of operation. In men younger than 70 years, there was no significant correlation between AP and the number of months after surgery ($n=35$, $y=-0.000889x+0.945$, $r=-0.223$, N.S.). A significant negative correlation was found between EstVBMD and the number of months ($n=35$, $y=-0.000237x+0.198$, $r=-0.365$, $P<0.05$) (Fig. 6-A). In men 70 years of age or older, there was no correlation between AP and the number of months after surgery ($n=6$, $r=-0.0548$, N.S.); similar results were obtained for EstVBMD ($n=6$, $r=-0.130$, N.S.) (Fig. 6-B). N.S., not significant.

and more than 10 years after operation. Hirano et al. (20) similarly found no difference in the rate of osteopathy among 0 to 1.9 years, 2.0 to 4.9 years, and 5.0 to 8.9 years after operation. In contrast, Tanaka et al. (19) showed that the incidence of osteopathy gradually rose as the postoperative duration of follow-up increased from 0 to 1 year (33.3%), 1 to 2 years (39.2%), 2.1 to 5 years (43.4%), and 5.1 to 10 years (49.9%). Kitahara et al. (30) showed a significant negative correlation between bone mineral density and the interval after operation in men 40 to 59 years of age in whom less than 30 months had elapsed since surgery and in women of similar age in whom less than 50 months had elapsed. Inoue et al. (28) demonstrated that bone marrow density was significantly lower in patients 2 to 5 years after gastrectomy, performed between 50 and 69 years of age, than in age-matched healthy subjects. Nihei et al. (29) reported that the bone mineral density index was significantly lower in patients 1 to 2 years after operation than in those less than 6 months after operation.

Since we assumed that men and women have a different pattern of change in bone mineral density after gastrectomy, bone mineral density was studied according to sex. When bone mineral density was compared between the sexes for the entire study group, both AP and EstVBMD were slightly, but not significantly, higher in men. Although there were no marked changes in bone mineral density according to age in men, however, both AP and EstVBMD were significantly lower in women 60 to 69 years of age than in those younger than 60 years. Kin et al. (31) reported that in healthy Japanese women bone mineral density as determined by DXA starts to decrease before menopause and decreases markedly after the age of 50 years. Arlot et al. (32) also showed that bone mineral density declines rapidly within 10 years after menopause. These findings indicate that women 60 years of age or older who undergo gastrectomy have a similar decrease in bone mineral density as that seen in age-matched healthy women; the effect of gastrectomy appears minimal.

To accurately evaluate changes in bone mineral density after gastrectomy, we examined the relation between bone mineral density and the number of months after operation after excluding elderly patients aged 70 years or older. Men showed a negative correlation between bone mineral density and the number of months after gastrectomy, whereas in women both AP and EstVBMD were independent of the interval after operation. These findings suggest that when the influence of aging is excluded bone mineral density gradually decreases after gastrectomy in men; the risk of osteopathy can thereby be forecast on the basis of the interval after gastrectomy, thereby permitting early therapy. In women, however, the rapid decrease in female hormone levels after menopause apparently outweighs the effects of gastrectomy with respect to bone mineral density. Menopausal status should therefore be confirmed in women who undergo gastrectomy, and therapy should be tailored to individual needs.

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和文抄録

胃切除術後の単位体積当たりの骨密度の変化
—Dual energy X-ray absorptiometory (DXA) 法による検討—

順天堂大学伊豆長岡病院　外科
矢吹　清隆，佐藤　浩一，前川　武男

越谷市立病院　外科
津村　秀憲，渡部　洋三

胃切除後の腰椎の骨密度の変化を dual energy X-ray absorptiometory (DXA) 法で測定し，単位体積当たりの計測値 (Estimated volumetric bone mineral density: EstVBMD) を求めることにより検討した．男女別に60歳未満，60歳代，70歳以上の群で比較すると，男性では 0.185 g/cm^3, 0.187 g/cm^3, 0.187 g/cm^3 と大差がなかった．一方，女性では 0.200 g/cm^3, 0.157 g/cm^3, 0.159 g/cm^3 と60歳未満の症例と比較し60歳代，70歳以上の症例では減少し有意差を認めた．70歳未満の症例で男女別に術後月数と骨密度との関係をみると，男性では経過期間とともに骨密度は減少し，負の相関関係 ($r=-0.365$, $P<0.05$) が認められたが，女性では両者は独立した関係であった．

70歳未満の男性では胃切術後に徐々に骨塩量が低下するが，女性では閉経後の女性ホルモン減少が強く骨代謝に現れるため胃切術後の影響が個々で異なることが示唆された．