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Evaluation of the effects of gastrectomy on the development of metabolic bone disease

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ABSTRACT

Background: Metabolic bone disease after gastrectomy is one of the complications leading to deterioration in quality of life. The exact mechanism of the metabolic bone disease remains unclear. To clarify the cause of metabolic bone disease after gastrectomy, we evaluated the associations between the method of gastrectomy and the development of metabolic bone disease in a rat model.

Methods: Rats were assigned to four groups as follows: (1) sham operation (control group); (2) resection of the glandular stomach with Billroth I reconstruction (RGBI group); (3) Roux-en-Y anastomosis preserving the secretory function of the whole stomach (PSRY group); and (4) total gastrectomy with Roux-en-Y reconstruction (TGRY group). In all groups, body weight, serum biochemistry (total protein, albumin, calcium, phosphorus, tartrate-resistant acid phosphatase, and bone alkaline phosphatase), bone density, and bone breaking strength were measured.

Results: Body weights and serum calcium levels were significantly lower in the three operation groups compared with the control group. Bone density was significantly lower in the PSRY and TGRY groups compared with the control group. Bone breaking strength was significantly lower in the three operation groups compared with the control group.

Conclusions: Surgical methods led to metabolic bone disease. However, exclusion of the duodenum from food passage had major influence to reduction in bone density and breaking strength. A stomach-preserving procedure and physiological reconstruction which enable food passage through duodenum and proximal jejunum contribute to mitigation of metabolic bone disease.

Introduction

Although the incidence of gastric cancer has declined, it remains one of the most common causes of cancer-related mortality worldwide. Surgical resection is the primary treatment for gastric cancer. The proportion of patients with early gastric cancer who are capable of long-term survival continues to increase due to the recent advances in diagnostic techniques. Therefore, some of the surviving patients suffer from sequelae caused by their surgical procedure. Major long-term complications after gastrectomy, such as dumping syndrome, reflux esophagitis, weight loss, malnutrition, and

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anemia caused by deficiency of iron and/or vitamin B_{12}, are well known.[1,2] Metabolic bone disease after gastrectomy is one of the complications leading to deterioration in quality of life because decreased bone quality results in pain and fractures. This disorder proceeds slowly and asymptomatically, becoming apparent 5-15 y after gastrectomy.[3] Metabolic bone disease reported to be observed in 20%-50% of patients after gastrectomy.[4] The proportion of elderly patients receiving gastrectomy has recently increased, and consequently, the risk of metabolic bone disease after gastrectomy is likely to have increased. In textbooks for orthopedics and endocrinology, the main cause of postgastrectomy metabolic bone disease is described as deficiency of vitamin D and calcium (Ca), leading to osteoporosis and osteomalacia due to a decrease in bone quality. It is speculated that the loss of gastric juice and gastric reservoir function, exclusion of food passage through the duodenum, and pancreatocibal asynchrony can lead to malabsorption of Ca and vitamins and malnutrition. Although various types of gastrectomy and reconstruction methods are performed clinically, the influence of these surgical procedures on bone metabolism remains unclear. The advantages and demerits of several surgical procedures have been discussed, but there is little available information on the surgical procedures from the viewpoint of bone metabolism. In fact, analysis of metabolic bone disease after gastrectomy is difficult in clinical cases, because the characteristics of the patients vary widely. Therefore, we planned our experiments using rat gastric surgery models, which have uniform backgrounds. To evaluate the influence of gastric juice and food passage route, we created several gastrectomized rat models similar to clinical gastric surgery. In this study, we focused on the association between the type of surgical intervention and the development of metabolic bone disease.

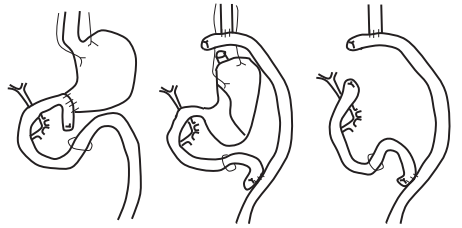
Materials and methods

Animals and surgical procedures

Twelve-wk-old Wistar male rats (Charles River Japan, Kanagawa, Japan) weighing approximately 400 g were used for the experiments. They were housed at three rats per cage and maintained under conditions of 22 ± 3°C room temperature and 55 ± 5% humidity with a 12-h/12-h light/dark cycle. They were fed a standard solid chow (CRF-1; Charles River Japan). Body weights were measured at the beginning of the study and then weekly thereafter. We followed the ARRIVE Guidelines (Animal Research: Reporting In Vivo Experiments) 18,[5] and the Animal Welfare Committee of Kanazawa University approved the experiments before the start of the study.

For evaluation of the association between the types of gastrectomy/reconstruction and postoperative metabolic bone disease, we created several surgical models. Before surgery, the rats were anesthetized by intraperitoneal injection of medetomidine, midazolam, and butorphanol. All operations involved a ventral midline celiotomy. Y.H. performed all surgical procedures. The stomach of the rat can be distinguished anatomically into a proximal part (forestomach) and a distal part (glandular stomach). The forestomach corresponds to the esophagus in humans, lacking the ability to secrete digestive juice, whereas the glandular portion most closely resembles the human stomach.

The rat with sham operation was defined as simple laparotomy with blunt manipulation of the viscera. In the rats with resection of the glandular stomach with Billroth I (B-I) reconstruction (RGBI; Fig. 1A), the glandular stomach was removed. The forestomach stump was then anastomosed to the duodenum near its cut end in an end-to-side fashion. The vagal nerve was preserved. These rats secrete no gastric juice, but their intestinal continuity is physiologically maintained including the duodenum and proximal jejunum. In the rats Roux-en-Y (RY) anastomosis preserving the stomach (PSRY; Fig. 1B), the total stomach and vagal nerve were preserved. The esophagus was cut, and the end remaining attached to the stomach was ligated. The jejunum was cut approximately 4-cm distal to the Treitz ligament, and the end closest to the stomach was ligated with suture. The oral esophagus was then anastomosed to the distal jejunum near its suture cut end in an end-to-side fashion. The proximal jejunal cut end was anastomosed to the jejunum approximately 5 cm distal from the esophagojejunal anastomosis in a side-to-side fashion. These rats secrete gastric juice, but the food also bypasses the stomach. In the rats with total gastrectomy with RY reconstruction (TGRY; Fig. 1C), both the glandular stomach and the forestomach were removed, and the duodenal stump was closed with sutures. The jejunum was cut approximately 4 cm distal to the Treitz ligament, and both ends were closed with sutures. The esophageal stump was anastomosed to the distal jejunum near its cut end in an end-to-side fashion. The proximal jejunal cut end was anastomosed to the jejunum at approximately 5 cm distal from the esophagojejunal anastomosis in a side-to-side fashion. The vagal nerve was not preserved. These rats secrete no gastric juice, and their food passage bypasses the duodenum and proximal jejunum. In all gastrectomy groups, anastomosis was carried out with interrupted full thickness stitches using 8-0 monofilament absorbable surgical sutures (Surgipro II Medtoronic, Dublin, Ireland). The rats received water for 3 days after the surgery,



	control	(A) RGBI	(B) PSRY	(C) TGRY
Acidity	+	-	+	-
Physiological GI continuity	+	+	-	-

Fig. 1 – Diagrams of the surgical procedures. (A) RGBI, (B) Roux-en-Y anastomosis with preserving the secretory function of the whole stomach, and (C) total gastrectomy with Roux-en-Y reconstruction (TGRY).