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学位論文題目	Effect of sleeve gastrectomy on body weight, food intake, glucose tolerance, and metabolic hormone level in two different rat models:Goto-Kakizaki and diet-induced obese rat  (2つの異なるモデルラット (GOTO-KAKIZAKI ラットと色餌誘発肥満ラット) における体重、食物摂取、耐糖能と代謝ホルモンレベルに対するスリーブ状胃切除の影響について)
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## 論文内容要旨

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学位論文題目	<p><b>EFFECT OF SLEEVE GASTRECTOMY ON BODY WEIGHT, FOOD INTAKE, GLUCOSE TOLERANCE, AND METABOLIC HORMONES LEVEL IN TWO DIFFERENT RAT MODELS: GOTO-KAKIZAKI AND DIET-INDUCED OBESE RAT</b></p> <p>(2つの異なるモデルラット (GOTO-KAKIZAKI ラットと色餌誘発肥満ラット) における体重、食物摂取、耐糖能と代謝ホルモンレベルに対するスリーブ状胃切除の影響について)</p>		
<p><b>INTRODUCTION</b></p> <p>Sleeve gastrectomy (SG) is usually indicated in obese patients with or without type 2 diabetes mellitus (T2DM), but it is still important question whether SG is appropriate only in the context of obesity—the condition for which it was originally developed—or whether lean people with insulin-deficient diabetes might also benefit. In the present study, we performed SG in Goto-Kakizaki (GK) and diet-induced obese (DIO) rats in order to compare the effects of SG on body weight, food intake, glucose tolerance, and metabolic hormones level in these two rat models that have distinct characteristics in beta-cell function and fat mass.</p> <p><b>MATERIAL AND METHODS</b></p> <p>SG was performed in GK and DIO rats. DIO rats were induced by feeding the Wistar rats with high fat diet during 12 weeks. SG was performed using the stapler Echelon TM 45 to lead to a drastic reduction of the gastric volume of about 70–80%. Body weight, food intake, and fasting blood glucose were monitored after surgery. Des-acyl ghrelin in fasting condition and blood glucose, insulin, and glucagon-like peptide-1 (GLP-1) levels during meal test were measured. Homeostatic model assessment (HOMA-IR) and insulinogenic index were examined.</p>			

## RESULTS and DISCUSSION

In both GK and DIO rats, body weight and food intake remained reduced in SG-treated rats compared with SO-treated rats throughout the duration of the study. In addition, fasting des-acyl ghrelin levels were significantly lower in SG-treated rats compared with those in SO-treated rats at 1 and 5 months after surgery.

In DIO rats, the improvement in glucose tolerance during meal test appeared clearly at three months after surgery and was associated with an increase in early insulin secretion and sensitivity. GLP-1 secretion was significantly increased during meal test in SG-treated rats. However, in GK rats, glucose tolerance was significantly improved during meal test at five months after surgery. Insulin and GLP-1 secretion were significantly augmented during meal test in SG-treated rats but there was no significant difference in HOMA-IR between SG and SO rats. These findings suggested that the mechanism of improvement in glucose tolerance after SG in two rat models may be different. In DIO rats, early insulin response during meal test was enhanced and insulin resistance was decreased after SG; whereas in GK rats, not only early insulin response but also total insulin secretion was augmented during meal test after SG but insulin sensitivity was not affected. In addition, our findings also advocated that beta-cell function might be considered a predictor of resolution of T2DM after SG.

## CONCLUSION

Taken together, in both GK and DIO rats with distinct characteristics in beta-cell function and fat mass, SG could improve glucose tolerance with different mechanisms: increased total insulin secretion or increased insulin sensitivity, respectively. The improvement in glucose tolerance was shown earlier in DIO rats than in GK rats.

## 学位論文審査の結果の要旨

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<p>減量手術の一つであるスリーブ状胃切除術は、近年その安全性や減量効果さらには肥満患者の糖尿病の改善効果の面から注目されている術式である。肥満患者に対して施行されてきたスリーブ状胃切除術 (SG) が、非肥満糖尿病患者に対しても効果があるかどうかは、臨床的に極めて重要な問題である。本研究では、膵β細胞機能と体脂肪量の異なった2種類のラット (GK および DIO) による SG モデルを作成し、体重・摂食量・糖代謝への影響を調べ、以下の点を明らかにした。</p> <ol style="list-style-type: none"> <li>1. GK と DIO のいずれのラットにおいても、SG により、meal test における GLP-1 とインスリンの分泌上昇を伴う耐糖能異常の改善が見られ、空腹時グレリン値は低下した。</li> <li>2. DIO では、SG 後にインスリン感受性が改善した。</li> <li>3. SG 後、GK よりも DIO において早く耐糖能異常が改善し、体重の増加は DIO よりも GK でより早くまた顕著であった。</li> </ol> <p>以上、GK と DIO のいずれにおいても、SG は GLP-1 とインスリンの分泌上昇を伴う耐糖能異常の改善を認めた。さらに耐糖能異常の改善は、GK よりも DIO で術後早期に確認された。</p> <p>本論文は、SG の非肥満糖尿病患者に対する効果の基礎研究として新しい知見を与えたものであり、最終試験として論文内容に関連した試問を受け合格したので、博士 (医学) の学位論文に値するものと認められた。</p> <p style="text-align: right;">(総字数 529 字)</p> <p style="text-align: right;">(平成 26 年 1 月 29 日 )</p>			