Three-Dimensional Computed Tomographic Volumetric Changes in Pancreas Before and After Living Donor Surgery for Pancreas Transplantation: Effect of Volume on Glucose Metabolism


ABSTRACT

In the present study, we aimed to compare the pancreas volumetric changes before and after living donor surgery for pancreas transplantation, using three-dimensional (3D) computed tomography (CT) and glucose metabolism. Pancreatic volume (PV) measurement using 3D CT was performed in 13 consecutive donors who underwent distal pancreatectomy for simultaneous living donor pancreas and kidney transplantation. PV was measured using a workstation before and 3 months after living donor operation. As the parameters of glucose metabolism, hemoglobin A1c (HbA1c) level, fasting plasma glucose (FPG) level, body mass index (BMI), homeostasis model assessment of insulin resistance (HOMA-IR), and insulinogenic index (IGI) were examined simultaneously with the PV measurement. The preoperative and postoperative PVs of pancreas was 30 ± 5 mL and 42 ± 9 mL, respectively. The postoperative PV was significantly higher than the preoperative PV ($P < .01$) and increased by approximately 40% at 3 months after surgery. The postoperative FPG and HbA1c levels were significantly higher than the preoperative values ($P < .01$). BMI decreased significantly after surgery ($P < .01$). No differences in HOMA-IR and IGI were noted between before and after surgery. Diabetes mellitus was not observed any of the 13 living donors during this period. Distal pancreatectomy for living donors caused an increase in the PV and maintained insulin resistance, but it was not sufficient to maintain glucose metabolism at the preoperative state.

The first living donor pancreas transplantation using a segmental pancreas (distal pancreas body and tail) was performed at the University of Minnesota on June 20, 1979 [1]. In 1994, the first simultaneous pancreas and kidney transplantation was also performed at the University of Minnesota [2]. Because of the severe shortage of deceased donors in Japan and the satisfactory outcomes of the living donor pancreas transplants that have been performed at the University of Minnesota, living donor pancreas transplantation was introduced in Japan on January 7, 2004 [3]. A recently developed laparoscopic surgical procedure has been found to be minimally invasive and safe and has attracted more living donors, thus increasing the donor pool for pancreatic transplantation [4]. Although the satisfactory outcome of living donor operation has improved, the possible deterioration of glycemic controls in living donors, as a result of distal pancreatectomy, has been a long-standing concern.

Computed tomographic (CT) examination after pancreas transplantation has been shown to be a useful method for detecting postoperative complications of pancreas allograft transplantation [5]. Three-dimensional (3D) CT volumetry of the liver, kidney, and lung is considered to be a reliable and accurate method for volumetric assessment [6-8]. Pancreatic volumetry using 3D CT has also been shown to provide accurate measurements for pancreas transplantation [9]. In patients with neoplasms, pancreatic volumetric assessment is a useful predictor of new-onset diabetes mellitus following distal pancreatectomy [10].

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However, in the case of pancreas from living donors, no data are available preoperative and postoperative volumetric assessments.

This present study describes 3D CT volumetric changes in pancreas before and after living donor pancreas transplantation and the effect of the volume of the reserved pancreas on the glucose metabolism of living donors.

**METHODS**

Of the 13 donors examined, 3 were men and 10 were women. The median donor age at transplantation was 56 years (range, 28–66 years). All the donors were healthy and fulfilled the previously reported stringent criteria for living donors for pancreas transplantation [3]. Pancreatic volume (PV) measurement using 3D CT was performed in 13 consecutive living donors who underwent distal pancreatectomy for simultaneous transplantation of the pancreas and kidney between May 2007 and April 2011. CT examination was performed using a 4-channel CT scanner (Aquilion Super 4, Toshiba, Tokyo, Japan), with intravenous administration of iodine contrast media. Each CT scan was obtained using the following settings: tube voltage, 120 kV; tube current, 220 mA; section thickness, 1 mm; reconstruction interval, 0.5 mm; pitch factor, 5.5; field of view, 32 to 40 cm; and matrix, 512 × 512. To accurately estimate the volume of the pancreatic parenchyma, contrast enhancement with an intravenous contrast medium was applied during 3D CT. The pancreatic head volume was outlined by the left edge of a superior mesenteric vein, and PV was measured before and 3 months after the living donor operation (Fig 1), using the workstation Virtual Place Fujin (AZE Software Inc., Tokyo, Japan).

As parameters of glucose metabolism, hemoglobin A1c (HbA1c) level, fasting plasma glucose (FPG) level, and body mass index (BMI) were examined simultaneously during PV measurement. The insulin resistance of a pancreas was evaluated by the homeostasis model assessment of insulin resistance (HOMA-IR) [11], which was calculated as \[ \text{FPG (mg/dL)} / \text{fasting insulin (\(\mu\text{U/mL}\))}/405 \], with lower values indicating a higher degree of insulin resistance. To evaluate the pancreatic \(\beta\)-cell function, we calculated the insulinoergic index (IGI) at 30 minutes during a 75-g oral glucose tolerance test (OGTT), as follows [12]:

\[
\text{IGI} = \frac{\text{insulin at 30 minutes}(\mu\text{U/mL})}{\text{insulin at 0 minutes}(\mu\text{U/mL})} \times \frac{\text{plasma glucose at 30 minutes}(\text{mg/dL})}{\text{plasma glucose at 0 minutes}(\text{mg/dL})}.
\]

This index can be used to evaluate the initial insulin secretion after glucose loading in healthy subjects and patients with impaired fasting glycemia/impaired glucose tolerance.

The statistical significance of the differences was analyzed by a paired \(t\) test, and \(P\) values of < .01 were considered to be statistically significant.

**RESULTS**

The mean PV of the entire pancreas was 66 mL. The mean PV of the preserved pancreatic head and tail were 30 mL (46%) and 36 mL (54%), respectively (Fig 2). No differences in preoperative 3D CT volumetric measurements were noted between the pancreatic head and body and tail. Almost half of the pancreatic parenchyma was obtained by distal pancreatectomy during living donor operation.

FPG levels increased from 88 ± 1 before surgery to 104 ± 6 after surgery (\(P < .01\)). Likewise, the postoperative HbA1c level was significantly higher as the compared to the preoperative HbA1c level (6.1 ± 0.4 vs 5.6 ± 0.2, respectively).

**Fig 1.** Preoperative images of three-dimensional computed tomography pancreatic volumetry. (A) The pancreatic head is outlined by the left edge of a superior mesenteric vein (arrow) conjoined with a splenic vein (arrowhead). (B) A pancreatic body-tail as an allograft.
respectively; \( P < .01 \). No cases of diabetes mellitus was noted in among all the 13 living donors during this period. The BMI decreased from 23.0 \( \pm \) 0.5 before surgery to 21.4 \( \pm \) 2.2 after surgery (\( P < .01 \)). No significant differences in HOMA-IR (1.3 \( \pm \) 0.7 vs 1.0 \( \pm \) 0.4, respectively) and IGI (1.1 \( \pm \) 1.1 vs 0.6 \( \pm \) 0.5, respectively) were noted between the values before and after surgery (Table 1).

The preoperative and postoperative PVs were 30 \( \pm \) 5 mL and 42 \( \pm \) 9 mL, respectively. The postoperative PV was significantly higher than the preoperative PV (\( P < .01 \)) and increased by approximately 40% at 3 months after surgery (Fig 3).

**CASE REPORTS**

The preoperative PV on 3D CT was 42 mL (Fig 4A), and the postoperative PV was 52 mL (Fig 4B) at 3 months after surgery, thus indicating an obvious increase in the living donor PV after distal pancreatectomy.

**DISCUSSION**

The effects of distal pancreatectomy on glucose metabolism and \( \beta \)-cell function of living donors have been studied [13–15]. Insulin secretion was found to be lower after distal pancreatectomy [13]. Our study showed that the IGI, calculated using the 75-g OGGT and used to assess \( \beta \)-cell function, did not decrease significantly and tended to decrease after donor surgery. Although FPG and HbA1c levels were reported to be significantly higher postoperatively than the values preoperatively, normal glucose and HbA1c levels were maintained [13–15]. In addition, our study demonstrated that plasma glucose and HbA1c levels increased significantly at 3 months after distal pancreatectomy and did not exceed the reference range. The effects of distal pancreatectomy on increased secretion levels have been limited to our donor operations.

Obesity is now a contraindication to living pancreas donation [15]. A living donor who is to undergo distal pancreatectomy should be strongly advised to avoid becoming obese. Our study showed the BMI of all the donors was maintained within the reference range, but decreased significantly after the operation. The HOMA-IR allows for a quantitative assessment of the contributions of fasting plasma insulin and glucose concentrations to insulin resistance. The HOMA-IR of our donors was maintained within normal levels. Thus the living donor operation did not diminish the ability of insulin resistance to maintain the postoperative body weight. These results on BMI and

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<th>Table 1. Glycemic Metabolism of Donors (( n = 13 )) Before and After Surgery</th>
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<td>Fasting plasma glucose (mg/dL)</td>
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<td>HbA1c (NGSP%)</td>
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<td>Body mass index (kg/m²)</td>
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Abbreviations: NGSP, National Glycohemoglobin Standardization supported by the National Institutes of Diabetes and Digestive and Kidney Diseases; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance.

*Statistically significant (\( P < .01 \)).
HOMA-IR may compensate for the decrease in insulin secretion after distal pancreatectomy.

Through 3D CT volumetry, we were able to estimate the volume of each allograft, such as that of the liver, kidney, and lung, and obtain additional information on preoperative allograft anatomical architecture [6–8]. The information is useful to determine the living allograft to be resected and postoperatively evaluate transplants. This technique could be used more widely to assess the preserved organ of living donors. Previous studies reported that the pancreatic weight in rats increased significantly with the increase in the volume of the preserved pancreas by distal pancreatectomy [16,17]. Bombesin, a tetradecapeptide hormone analogue of a mammalian gastrin-releasing peptide, plays a role in pancreatic growth and regeneration. When no bombesin was administered, the pancreatic weights in rats increased twice as much as the preoperative values after 90% of the PV was resected by distal pancreatectomy [17].

In humans, distal pancreatectomy did not induce an increase in PV, as evidenced on 3D CT [18]. However, this report included cases of chronic pancreas, pancreatic carcinoma, and pancreatic metastasis, but did not include normal pancreas. Our study demonstrated that the normal pancreas that fulfilled the stringent donor criteria had apparently exhibited increased PV on 3D CT after distal pancreatectomy. PV assessment was used as a predictor of new-onset diabetes mellitus after distal pancreatectomy for pancreatic neoplasm [10]. This study conclude that preoperative HbA1c levels higher than 5.7% and a pancreatic resection rate higher than 44% were independent risk factors for new-onset diabetes mellitus after distal pancreatectomy. Our study showed that in the cases with preoperative HbA1c levels lower than 5.7% and mean pancreatic resection rates of almost 50%, no new-onset diabetes mellitus was observed. Distal pancreatectomy for living donors resulted in an increase in the volume of the reserved pancreas and maintenance of insulin resistance; however, these effects were not to sufficient to maintain the preoperative insulin secretion levels. Recently, local in vivo GSK3β knockdown was found to promote β-cell and acinar-cell regeneration in 90% pancreatectomized rats [19]. Intrapancreatic GSK3β knockdown leads to increased β-cell mass by promoting β-cell proliferation and differentiation. In the near future, this gene therapy may be helpful to promote human β-cell mass regeneration after donor distal pancreatectomy to maintain glucose metabolism.

REFERENCES


