Bile acid, glucose, lipid profile, and liver enzyme changes in pre-diabetics after sleeve gastrectomy

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Abstract

Background

Few articles have studied pre-diabetes after sleeve gastrectomy. Bile acid, and lipid metabolism remains inconsistent in post-bariatric patients.

Objective

To explore bile acid and glucose, lipid, and liver enzyme changes in different diabetic status underwent sleeve gastrectomy. To discuss the impact of bariatric surgery and its potential benefits to pre-diabetics

Methods

202 overweight and obese patients underwent bariatric surgery between January 2016 and October 2018 in our hospital were retrospectively reviewed. They were divided into Pre-diabetes (n=32), Non-diabetes (n=144), and Diabetes (n=26) and analyzed respectively. Data of glucose and lipid metabolism were collected from medical records from baseline and each follow-up visit.

Result

Significant improvement in body weight, glucose and lipid metabolism, and liver enzyme at P≤0.05 in prediabetics were found throughout first year post-op. Improvement of glycemic control was first seen in a month post op, followed by persistent improvement in the next 12 months. Total bile acid (TBA) decreased, associated with ALT improvement, in pre-diabetes 1-year post-surgery. There was no significant differences in HbA1c, glucose, and triglycerides (TG) between Pre-diabetics and T2DM nor between prediabetics and non-diabetics at 12 months post-surgery.

Conclusion

LSG is highly effective in interfering glucose and lipid metabolism as well as total bile acid of prediabetics in the first year post op. Thus, LSG is indeed an alternative for overweight and obese prediabetics

Background

Obesity is a worldwide health problem that affects children, adolescents, and adults and is accompanied by comorbidities such as hypertension, dyslipidemia, type 2 diabetes, cancer, osteoarthritis, and sleep apnea [1]. Especially, Type 2 diabetes (T2DM) is a global pandemic, with a global prevalence of about 8.3%, and is expected to rise to 10% by 2030 [2]. The correlation between T2DM and obesity was established. These two risk factors are steadily increasing in the general population, which may be the result of lifestyle changes [3]. The majority paid close attention to the risk of T2DM, but few concerned with pre-diabetes. A combination of FPG of 6.1 to 6.9 mmol / L and HbA1C of 6.0% to 6.4% predicts that
100% will develop type 2 diabetes within 5 years [4]. Only a few of study had been researched for the patient with pre-diabetes after sleeve gastrectomy, which is a type of bariatric surgery.

BA is a complex metabolic molecule that directly affects not only lipid metabolism but also intestinal peptide secretion and blood glucose control [5]. BAs are considered to be important mediators of weight loss and metabolic changes after bariatric surgery [6-9], and different proportions of BAs are related to different characteristics of glucose metabolism [10, 11]. Most studies report increased BA concentrations after bariatric surgery [12, 13], but others reveal inconsistent changes in BA scores [14-16].

In our study, we explored the change of glucose and lipid metabolism for overweight and obese prediabetics who underwent LSG and discussed the change of bile acids for the Pre-diabetes patient.

**Methods**

**Study design and Patient Selection**

A retrospective observational study of a collected database was conducted in patients undergoing LSG in the Department of metabolic and obesity surgery of the First Affiliated Hospital of Jinan University (Guangzhou, China) between January 2016 and October 2018. Inclusion criteria were body mass index (BMI) $\geq 32.5$ kg/m² or $\geq 27.5$ kg/m² with one or more co-morbid conditions (hypertension, type 2 diabetes, dyslipidemia, or OSA) who failing managed by lifestyle modification. Exclusion criteria were patients with a history of bariatric surgery or cholecystectomy. Moreover, patient with Pre-diabetes was diagnosed according to CAD guideline [17], whom states either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), with 6.0-6.4% HbA1c falling into the prediabetes diagnosis criteria. Patients are divided into 3 groups, T2DM, pre-diabetes and non-diabetes according to their diabetes status. All participants had been informed and consented to involved in this study.

All patients completed a systematic route examination investigation before bariatric surgery and each follow-up visit at 1, 3, 6, 12 months post op. It includes routine physical examination, weight, obesity-related comorbidities investigation, and route laboratory tests. Data, including age, gender, body weight, body height, BMI, surgery methods, HbA1c, insulin, C-peptide, fasting glucose, total bile acid (TBA), cholesterol (CHOL), triglyceride (TG), LDL-c, HDL-c, alanine transaminase (ALT), aspartate transaminase (AST), are collected from medical records from baselines and its following visits.

**Postoperative Management Follow-up**

All patients, underwent surgery, are suggested follow-up revisit for physical examination at 1, 3, 6, 12 months. They were advised to take calcium tablet (Caltrate®), which includes 600 mg calcium and 125 IU vitamin D3; and multivitamin supplementations (Centrum®), which includes 162 mg calcium and 400 IU vitamin D, 0.4 mg folate, 6µg vitamin B12, 18 mg iron, 36.3 mg chlorine, 125 mg phosphorus, 40 mg potassium, 100 mg magnesium, 5000 IU vitamin A, 15 mg zinc, 20 mg nicotinamide, 2.5 mg manganese, 1.5 mg vitamin B1, 25 µg chromium, 1.7 mg vitamin B2, 25µg molybdenum, 2 mg vitamin B6, 25µg
selenium, 60 mg vitamin C, 5µg nickel, 10µg tin, 25µg vitamin K1, 10µg silicon, 30µg biotin, 2 mg copper, and 10µg vanadium. Lifelong prescription of both supplements was recommended.

**Surgery Technique**

All surgical procedures were performed laparoscopically under standardized methodology [18] by an experienced surgical experts. Stomach is resected from the starting point for stapling, approximately 2-4 cm above the pylorus, followed by entire fundus resection.

**Statistical Analysis**

The data were reported as mean, standard deviation, and percentage. Statistical Product and Service Solution version 19.0 (SPSS 19.0, SPSS Inc., Chicago, IL) was used for data analysis. Student's t-test or Mann–Whitney test analyzed the continuous data. P ≤ 0.05 was considered statistically significant. The Pearson or the Spearman coefficients were used for correlation analyses. Excel illustrated line chart for listing variations of examined items.

**Results**

202 patients undergoing sleeve gastrectomy were presented in our center from January 2016 to October 2018. Having excluded 8.9% (n=18) individuals, whom presented with a history of cholecystomy, the rest of 184 individuals and theirs clinical characteristics were listed in Table 1. 16% (n=32) of patients was diagnosed as Pre-Diabetes prior bariatric surgery. 12 out of 26 diabetics were newly diagnosed. Patients with a history of diabetes were managed with either oral anti-glycemic agents or insulin alone or with a combination of oral agents and insulin. The medication was adjusted according to glycemic status on each follow-up visit. Average BMI of the bariatric patients decreased significantly from 36.5 kg/m² at baseline to 25.5 kg/m² at 1-year post-surgery. Table 1 revealed that pre-op Pre-diabetics had substantially greater BMI compared to the other groups. Subgroup analysis of bile acid, glycemic status, lipid profile and liver enzymes in the course of time were demonstrated in Table 3.

**Pre-Diabetes**

During 1-year post-surgery, patients with pre-diabetes were followed by a significantly continued reduction in weight, BMI, HbA1c, insulin, C-peptide, glucose, and TG (P ≤ 0.05) revealed in Table 2. There was no significant difference in CHOL during 1-year post-surgery. The total bile acid concentration was significantly different for 1-year post-surgery. HDL was significantly increasing after 6 months of post-surgery (P ≤ 0.05). AST and ALT were significantly decreasing after post-surgery in 3, 6 and 12 months. Improvement in glycemic control and body weight was seen already 1 month after surgery, with continued improvement during the next 12 months. Besides, Spearman's Rhoa, in table 4, revealed a correlation between the change of bile acid and ALT improvements.

Comparing between the patient with different glucose status
Prior bariatric surgery, there was a significant difference in HbA1c and Glucose between Pre-diabetes and Diabetes at significant level when \( P \leq 0.05 \) described in Table 3. After 6 months post-operation, both groups’ glucose control was notably improved (Fig 1a,b). There was no significant differences in HbA1c and glucose between all groups at 12 months post-operation. The change of glucose between Pre-Diabetes and Type 2 Diabetes subjects significantly differed after 1-year post-operation (\( P \leq 0.05 \)). In terms of lipid metabolism, there was no significant differences between Pre-diabetes and Diabetes after bariatric surgery (Table 3 & Fig 1c). The liver enzymes were improved post-op; but the value of Pre-diabetics was higher than the Non-diabetics at the baseline(Fig 2)

Pre-operation BA, CHOL, LDL and TG of Pre-diabetics and non-diabetics was not significantly different revealed in Table 3. At 6 months post-operation, both groups’ glucose control, lipid profile and liver enzyme were remarkably improved (Fig 1a,b & Fig 2). The findings of body weight, glucose and lipid metabolism in the Pre-diabetics shared some degree of similarities in Non-Diabetic groups at 1 year post op. (Table 3 & Fig 1). The change in HbA1c and glucose between Pre-Diabetes and Non-Diabetes subjects were significantly different (\( P \leq 0.05 \)) at any interval after post-operation. At 1 year post-surgery, of pre-diabetes & diabetes, glucose control was at the normal standard and other examined items have been improved.

**Discussion**

Majority of researches have proven that bariatric surgery is an alternative for improving glucose and lipid metabolism. Remission of diabetes correlates with weight reduction [19]. Bariatric surgery is an excellent solution to Diabetes remission and weight reduction in most cases [20]. However, only few studies had researched on the impact of sleeve gastrectomy on pre-diabetics. In this study, the changes of glucose, lipid profile, bile acids of pre-diabetes, who underwent LSG, were explored and discussed.

Having a large meta-analysis [21] and recent observational studies [20] proven improvement in glucose metabolism had a correlation with weight reduction. Similarly, reduction of food intake capacity via bariatric surgery aided to weight loss as seen as continuous loss of weight in all groups, non-diabetics, diabetics, pre-diabetics, during the course of a year post-op. In terms of glycemic status, expectedly initial HbA1c and fasting glucose of prediabetics appeared to be significantly different in comparison to non-diabetics alone and T2DM alone. Improvement of glycemic control and body weight in pre-diabetics and diabetics began at the first month post-op and persisted in the next 12 months. This corresponded to Rubio-Almanza et al, who suggested that bariatric surgery improved glycemic control and obesity comorbidities in the pre-diabetes patient [22]. Besides, nearly 70% of pre-diabetics in our centre was treated by LSG. Within the course of study, remarkably improvement of glycemic state was observed in both diabetics and pre-diabetics. LSG therefore is an effective alternative for pre-diabetics, whom failing managed by lifestyle modification, to assist with both weight loss and glycemic control, thus delaying and preventing the progression of T2DM [23]. The advantage of LSG is minimal invasive, relatively low risks and few complications, and cost effective meanwhile highly effective in delaying and preventing the
obesity and T2DM comorbidities and theirs irreversible neurovascular complications in advance [24]. Hence, LSG shall be encouraged in pre-diabetics.

Epidemiological and clinical studies have not only shown that HDL-C is negatively correlated with the incidence of atherosclerotic related disease, but also recently suggests that some effects of bariatric surgery take place speedily after surgery as it may involve increased HDL levels [25-27]. Similarly, HDL, 'good cholesterol' was significantly increased in prediabetics after 6 months LSG operation. HDL increased is thought to associate with improvement of hepatic insulin sensitivity [28]. This perhaps explains the improved glycemic status after bariatric surgery. Further research may be necessary to reveal the mechanism of how HDL affect glucose metabolism.

Bile acids are derivatives of cholesterol synthesized in the hepatocyte, thus bile acid synthesis is a regulator of body cholesterol. Initial mean concentration of BA in diabetics and prediabetics was 3 µmol/L higher than the western [29-32]. The cause of high level of bile acid reminded unclear. Fatty liver, race, glycemic control or lipid profile may possibly contribute to the cause, resulting as compensatory bile acid secretion. Bile acid of prediabetics significantly reduced by the first year post-op. Some literatures indicated an increase in bile acids strongly correlates with the improvement in glucose and lipid metabolism [29, 30], but Robert E et al [32]do not support the hypothesis that bile acids are key mediators of the early increase in postprandial GLP-1 and PYY secretion for improvement in glucose metabolism in post-bariatric patients. Besides, Hilde Risstad et al [31] indicated form data that bile acids had no significant change in 1-year post-bariatric patients but significantly increased after 5 years. It is proved that bile acids are not key mediators for the improvement of glucose metabolism in early post-bariatric patients. Similarly, our results do not suggest that bile acid attributed to the rapid improvement in glycemic control seen shortly after surgery.

Regarding to lipid metabolism, this study revealed that triglyceride (TG) significantly continued to decrease. The fact that bile acid was synthesized and secreted by hepatocytes, therefore, liver function directly affected synthesis of bile acids. Clinically, ALT and AST are sensitive indicators of liver damage. ALT & AST reduced in this study, indicating an improvement of liver function after metabolic surgery. Additionally, there is a correlation between the change of bile acid and ALT in prediabetics.

Some limitations are included in this study. At first, bariatric surgery is still in the developing stage in China, postoperative regular follow-up has not been paid close attention to some patients, resulting in a high rate of loss to follow-up; therefore, the small postoperative sample size was shown. Besides, our study was a short-term follow-up study, but long-term follow up will be continued. Third, our result only reveals some clinical phenomenon, further researches are necessary to consider pre-diabetes as a criterion for metabolic surgery and long-term effect after metabolic surgery.

**Conclusion**

LSG is highly effective in improving glucose and lipid metabolism of pre-diabetics and diabetics. LSG is indeed alternative for pre-diabetics and shall be encouraged to prevent and delay the onset of diabetics.
and its irreversible neurovascular complications. Evidence of this study does support the phenomenon of total bile acid reduction during the course of first year post-LSG surgery.

**Abbreviations**

<p>LSG is highly effective in improving glucose and lipid metabolism of pre-diabetics and diabetics. LSG is indeed alternative for pre-diabetics and shall be encouraged to prevent and delay the onset of diabetics and its irreversible neurovascular complications. Evidence of this study does support the phenomenon of total bile acid reduction during the course of first year post-LSG surgery.</p>

**Declarations**

**Ethics approval and consent to participate:**

Ethical approval was waived by the local Ethics Committee (Ethics Committee of the First Affiliated Hospital of Jinan University) in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

**Consent for Publication:**

Not applicable.

Availability of data and material: The datasets generated and analysed during the current study are not publicly available as the data also forms part of an ongoing study but are available from the corresponding author on reasonable request.

**Competing interests:**

The authors declare that they have no competing interests.

**Funding:**

Not applicable.

**Authors' contributions:**

JGY and BSG and CCW performed the bariatric surgery on all 202 patients. TKM, SFH, THC, JZP, and HYA were major contributors in writing the manuscript and analyzed the data. FZC, CQL, WJL, and LLH collected the data. And all authors contributed to the follow up of patients. All authors have read and approved the submitted manuscript.

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Tables

Table 1 The baseline of clinical characteristic of this study (excluded Cholecystomy)
| Variables           | Pre-Diabetes | Non-Diabetes | Diabetes   |
|---------------------|--------------|--------------|------------|
| Subjects(n=32)      |              |              |            |
| Gender(Male/Female) | 9(28.1%)/23(71.9%) | 31(21.5%)/113(78.5%) | 14(53.8%)/12(46.2%) |
| Age                 | 29.9±10.73   | 27.29±8.61   | 30.92±9.07 |
| Weight(Kg)          | 107.8±22.6   | 99.8±19.8    | 111.3±23.0 |
| BMI                 | 37.5±5.2     | 36.2±4.82    | 36.9±4.01  |
| HbA1c(%)            | 6.41±1.09    | 5.39±0.35    | 7.2±1.14   |
| Insulin(pmol/L)     | 26.5±12.5    | 19.9±12.3    | 23.8±7.9   |
| C-peptide(ug/L)     | 3.8±1.08     | 3.25±1.31    | 4.39±2.74  |
| Glucose(mmol/L)     | 5.9±1.03     | 5.08±0.53    | 8.3±2.67   |
| TBA(umol/L)         | 4.3±4.07     | 4.06±4.69    | 3.77±2.2   |
| CHOL(mmol/L)        | 5.1±0.99     | 4.9±0.89     | 5.2±1.47   |
| TG(mmol/L)          | 2.3±2.21     | 1.71±0.91    | 2.23±1.06  |
| LDL(mmol/L)         | 3.2±0.68     | 3.02±0.74    | 3.5±0.97   |
| HDL(mmol/L)         | 0.99±0.22    | 1.1±0.29     | 1.0±0.16   |
| ALT(U/L)            | 69.2±41.2    | 41.7±40.89   | 74.4±47.2  |
| AST(U/L)            | 40.0±22.7    | 26.8±18.59   | 45.1±26.8  |

Table 2 The variable at baseline and after bariatric surgery in Pre-Diabetes patient
|                      | Pre-operative | 1 Month    | 3 Months   | 6 Months   | 1 Year     |
|----------------------|---------------|------------|------------|------------|------------|
| Weight(Kg)           | 107.8±22.6    | 95.3±14.3a | 87.8±16.7a | 73.6±7.26a | 74.2±6.61a |
| BMI                  | 37.5±5.2      | 33.6±4.3a  | 30.9±5.02a | 25.9±2.48a | 26.1±2.53a |
| HbA1c(%)             | 6.2±0.79      | 5.7±0.4a   | 5.3±0.3a   | 5.2±0.53a  | 5.3±0.2a   |
| Insulin(pmol/L)      | 26.5±12.5     | 13.9±10.5a | 10.7±5.97a | 7.3±2.92a  | 5.7±3.1a   |
| C-peptide(ug/L)      | 3.8±1.08      | 2.7±1.14a  | 2.5±0.91a  | 2.4±0.85a  | 1.7±0.49a  |
| Glucose(mmol/L)      | 5.9±1.03a,c   | 5.12±0.66a | 5.1±0.71a  | 5.1±1.08a  | 4.9±0.37a  |
| TBA(umol/L)          | 4.3±4.07      | 3.08±2.37  | 2.3±1.56   | 2.04±0.87a | 1.93±0.65a |
| CHOL(mmol/L)         | 5.1±0.99      | 4.48±0.9   | 4.7±0.67   | 5.2±0.76   | 5.06±0.72  |
| TG(mmol/L)           | 2.3±2.21      | 1.31±0.41a | 1.27±0.35a | 1.12±0.25a | 0.75±0.19a |
| LDL(mmol/L)          | 3.2±0.68      | 2.75±0.78  | 3.06±0.56  | 3.4±0.58   | 2.82±0.43  |
| HDL(mmol/L)          | 0.99±0.22     | 1.05±0.8   | 1.0±0.22   | 1.18±0.21a | 1.38±0.17a |
| ALT(U/L)             | 69.2±41.2     | 48.6±23.2  | 26.2±13.59a | 15.3±6.67a | 12.86±5.13a |
| AST(U/L)             | 40.0±22.7c    | 38.6±17.96 | 21.9±8.52a | 18.02±9.62a | 17.9±4.06a |

\( ^aP \leq 0.05 \) versus pre-operative within group.

Table 3 The variable at baseline and after bariatric surgery between the Diabetes status of patient
|                  | Pre-operative | 1 Month    | 3 Months   | 6 Months   | 1 Year      |
|------------------|---------------|------------|------------|------------|-------------|
| **Weight (Kg)**  |               |            |            |            |             |
| Pre-Diabetes     | 107.8±22.6    | 95.3±14.3c,d| 87.8±16.7b,c,d | 73.6±7.26  | 74.2±6.61d  |
| Diabetes         | 111.3±23.0    | 94.3±15.96 | 85.16±32.3 | 71.96±9.59 | 78.2±11.76  |
| Non-Diabetes     | 99.8±19.8     | 84.9±15.01 | 80.13±15.3 | 73.85±18.69| 67.33±10.84 |
| **BMI**          |               |            |            |            |             |
| Pre-Diabetes     | 37.5±5.2      | 33.6±4.3c  | 30.9±5.02  | 25.9±2.48  | 26.1±2.53c,d|
| Diabetes         | 36.9±4.01     | 33.5±4.13  | 27.89±3.99 | 24.46±2.59 | 25.59±3.33  |
| Non-Diabetes     | 36.2±4.82     | 31.31±4.15 | 29.21±4.323| 25.74±3.76 | 25.34±3.55  |
| **HbA1c (%)**    |               |            |            |            |             |
| Pre-Diabetes     | 6.2±0.79a,c   | 5.7±0.4a,c,d| 5.3±0.3b,c,d | 5.2±0.53d  | 5.3±0.2d    |
| Diabetes         | 7.2±1.14      | 6.4±0.56   | 5.3±0.4    | 4.9±0.4    | 5.08±0.3    |
| Non-Diabetes     | 5.39±0.35     | 5.2±0.3    | 5.02±0.3   | 5.09±0.27  | 5.09±0.23   |
| **Insulin (pmol/L)** |           |            |            |            |             |
| Pre-Diabetes     | 26.5±12.5c    | 13.9±10.5  | 10.7±5.97c,d | 7.3±2.92a  | 5.7±3.1b,d  |
| Diabetes         | 23.8±7.9      | 17.9±10.99 | 12.05±6.9  | 7.42±5.03  | 6.75±3.34   |
| Non-Diabetes     | 19.9±12.3     | 9.3±5.7    | 7.58±4.07  | 11.39±19.6 | 5.8±3.11    |
| **C-peptide (ug/L)** |         |            |            |            |             |
| Pre-Diabetes     | 3.8±1.08c     | 2.7±1.14b  | 2.5±0.91   | 2.4±0.85   | 1.7±0.49d   |
| Diabetes         | 4.39±2.74     | 4.08±1.68  | 2.75±0.98  | 2.3±0.99   | 1.97±0.67   |
| Non-Diabetes     | 3.25±1.31     | 2.44±1.07  | 2.17±0.82  | 2.4±2.5    | 1.6±0.6     |
| **Glucose (mmol/l)** |             |            |            |            |             |
| Pre-Diabetes     | 5.9±1.03a,c   | 5.12±0.66a,d| 5.1±0.71b,c,d | 5.1±1.08d  | 4.9±0.37b,d |
| Diabetes         | 8.3±2.67      | 6.2±1.26   | 5.52±0.81  | 5.3±0.36   | 4.7±0.46    |
| Non-Diabetes     | 5.08±0.53     | 4.96±0.51  | 4.9±0.47   | 4.9±0.51   | 4.74±0.39   |
| **TBA (umol/L)** |               |            |            |            |             |
| Pre-Diabetes     | 4.3±4.07      | 3.08±2.37  | 2.3±1.56   | 2.04±0.87a,b | 1.93±0.65   |
| Diabetes         | 3.77±2.2      | 2.6±1.11   | 2.8±1.57   | 4.33±1.71  | 3.74±3.0    |
|                      | CHOL (mmol/L) | TG (mmol/L) | LDL (mmol/L) | HDL (mmol/L) | ALT (U/L) | AST (U/L) |
|----------------------|--------------|-------------|--------------|--------------|-----------|-----------|
| **Non-Diabetes**     | 4.06±4.69    | 3.47±3.43   | 2.57±2.79    | 4.36±7.28    | 2.64±1.79 |           |
| **Pre-Diabetes**     | 5.1±0.99     | 4.48±0.9    | 4.7±0.67     | 5.2±0.76     | 5.06±0.72 |           |
| **Diabetes**         | 5.2±1.47     | 4.62±0.39   | 4.83±0.84    | 4.9±0.7      | 4.71±0.77 |           |
| **Non-Diabetes**     | 4.9±0.89     | 4.37±0.83   | 4.84±0.87    | 4.9±0.99     | 4.87±0.81 |           |
| **Pre-Diabetes**     | 5.1±0.99     | 4.48±0.9    | 4.7±0.67     | 5.2±0.76     | 5.06±0.72 |           |
| **Diabetes**         | 5.2±1.47     | 4.62±0.39   | 4.83±0.84    | 4.9±0.7      | 4.71±0.77 |           |
| **Non-Diabetes**     | 4.9±0.89     | 4.37±0.83   | 4.84±0.87    | 4.9±0.99     | 4.87±0.81 |           |

**ALT (U/L)**

| **Non-Diabetes**     | 69.2±41.2c   | 48.6±23.2c  | 26.2±13.59cd | 15.3±6.67d   | 12.86±5.13 |           |
| **Pre-Diabetes**     | 74.4±47.2    | 55.87±32.64 | 31.21±18.09  | 21.2±11.76   | 18.9±9.43  |           |
| **Diabetes**         | 41.7±40.89   | 34.1±26.43  | 18.23±11.56  | 18.77±15.73  | 14.69±5.31 |           |
| **AST (U/L)**

| **Non-Diabetes**     | 40.0±22.7c   | 38.6±17.96c | 21.9±8.52d   | 18.02±9.62d  | 17.9±4.06  |           |
| **Pre-Diabetes**     | 45.1±26.8    | 38.9±19.8   | 25.28±9.19   | 18.8±8.55    | 18.1±5.51  |           |
| **Diabetes**         | 26.8±18.59   | 26.9±12.45  | 20.51±16.24  | 18.63±12.23  | 16.94±3.68 |           |

\[ a \leq 0.05 \text{ Pre-Diabetes versus Diabetes at the same time point.} \]

\[ b \leq 0.05 \text{ The change of concentration between Pre-Diabetes and Diabetes.} \]

\[ c \leq 0.05 \text{ Pre-Diabetes versus Non-Diabetes at the same time point.} \]
The change of concentration between Pre-Diabetes and Non-Diabetes

Table 4 Correlation analyses in the Pre-diabetes of fasting serum of total bile acids, fasting serum lipids and measures of glucose metabolism for 1 years

| Change from baseline to 1 year | Spearman's Rhoa | P value |
|-------------------------------|-----------------|---------|
| Change in total bile acid concentrations |                 |         |
| Gender                        | -0.27           | 0.47    |
| Age                           | -0.38           | 0.32    |
| Weight(Kg)                    | -0.12           | 0.78    |
| BMI                           | -0.43           | 0.29    |
| HbA1c(%)                      | 0.16            | 0.71    |
| Insulin(pmol/L)               | -0.02           | 0.95    |
| C-peptide(ug/L)               | -0.21           | 0.61    |
| Glucose(mmol/L)               | 0.09            | 0.81    |
| CHOL(mmol/L)                  | -0.15           | 0.7     |
| TG(mmol/L)                    | 0.50            | 0.16    |
| LDL(mmol/L)                   | -0.58           | 0.27    |
| HDL(mmol/L)                   | -0.40           | 0.31    |
| ALT(U/L)                      | 0.67            | 0.04*   |
| AST(U/L)                      | 0.38            | 0.31    |

Figures
Figure 1

The concentration of HbA1c(A), glucose(B) and TG(C) in different diabetes status of patients before, 1 month, 3 months, 6 months and 12 months after surgery
Figure 2

The concentration of ALT(A) and AST(B) in different diabetes status of patients before, 1 month, 3 months, 6 months and 12 months after surgery

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- MakPrediabeteschecklist.docx