

# Temporal improvements in total bile acid levels following laparoscopic sleeve gastrectomy

## Introduction

- Type 2 diabetes (T2DM) and obesity are conditions associated with significant morbidity and mortality predominantly from associated chronic diseases
- Laparoscopic sleeve gastrectomy (LSG) is a relatively safe and cost-effective bariatric procedure that has demonstrated successful weight loss and improved physiological alterations
- Underlying mechanisms for these metabolic and hormonal improvements are not completely understood, but direct manipulation of bile acid (BA) flow to the mid-jejunum by LSG has been proposed to influence these changes

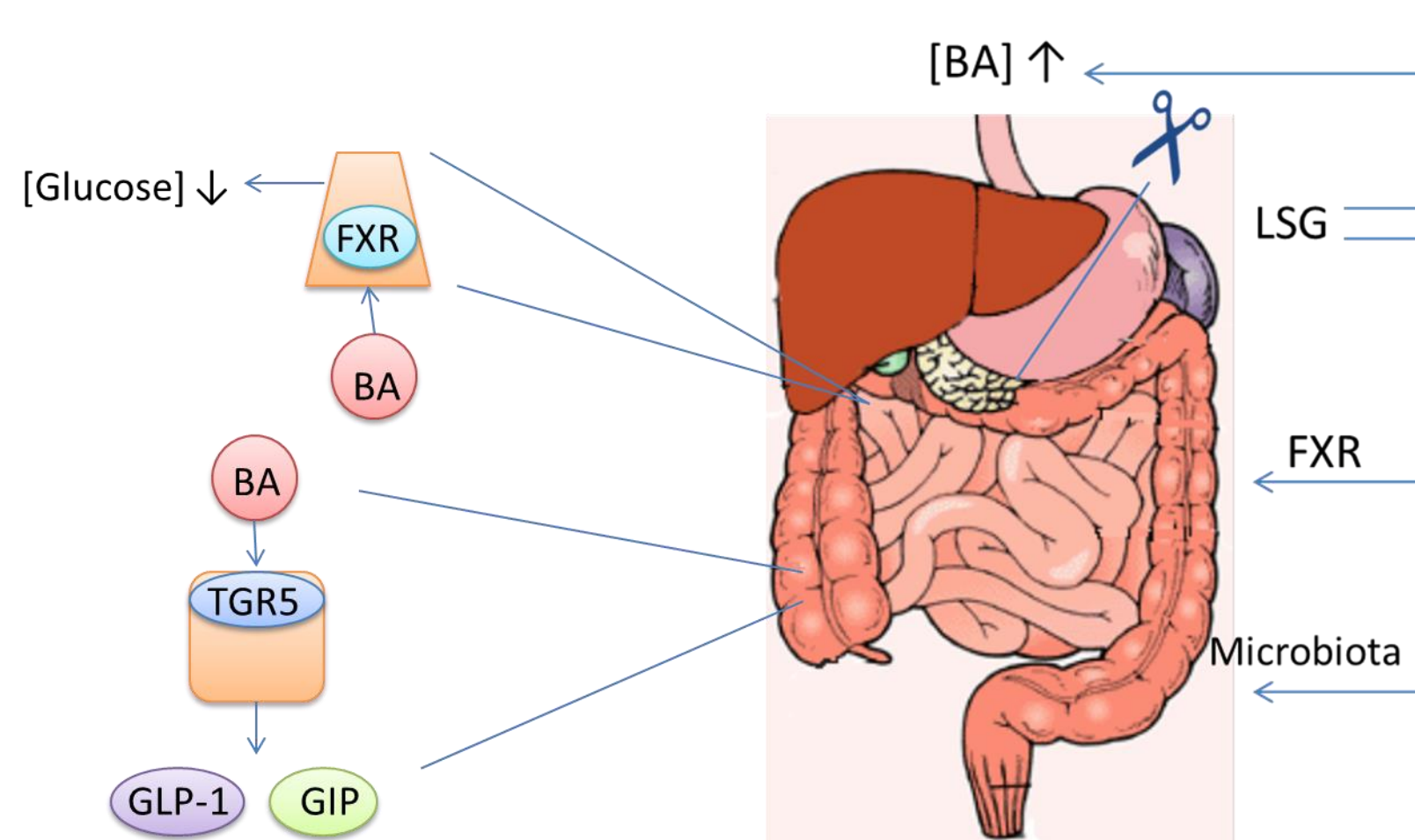


Figure 1  
Demonstration of how increased bile acids following LSG can influence whole-body metabolism

- Increased bile acid levels following LSG act on farnesoid X receptor (FXR) and its associated G-protein receptor in both the liver and intestines, reducing endogenous glucose
- Furthermore, bile acids may cause the modulation of the gastric peptides glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), both of which are mechanistically linked to changes in the microbial ecology of the gut

## Aims

- To investigate both static and dynamic measures of total bile acids in a cohort of subjects with impaired glucose homeostasis undergoing LSG

## Methods

- Participants (n=16) underwent a planned LSG procedure at the Welsh Institute of Metabolic & Obesity Surgery (WIMOS) at Morriston Hospital, Swansea, UK
- All participants underwent a standard 75g oral glucose tolerance test before surgery, and 1 and 6 months post-operatively
- Bile acid concentrations were determined using a commercially available colorimetric assay at 0 and 2 hour

## Conclusions

- Results show an accumulative increase in post-prandial total bile acids following LSG at both post operative visits
- This increase could have beneficial effects on the FXR pathway resulting in significant lowering of endogenous glucose levels
- More investigation is needed to understand the connection between bile acids, metabolic improvements and gut microbiota

## Results

- Significant reductions were observed in weight at both 1 month and 6 months post-operatively (16.5kg and 32.2kg respectively; p=0.011) (Table 1)
- Significant reductions were also observed for waist and hip circumference, HbA1c and fasting glucose and insulin concentrations (Table 1)
- Fasting total bile acid levels were not significantly different between post-operative visits (Table 1)

Table 1 Clinical and biochemical measurements

	Baseline	1 month	6 months	p-value
Weight (kg)	148.3 (31.3)	131.8 (26.5)	116.1 (26.8)	<b>0.011</b>
BMI (kg/m <sup>2</sup> )	49.4 (7.1)	44.1 (6.0)	38.9 (6.6)	<b>&lt;0.001</b>
Waist (cm)	140 (18.9)	130 (17.8)	119 (19.6)	<b>0.013</b>
Hip (cm)	149 (13.1)	137 (12.0)	129 (14.0)	<b>&lt;0.001</b>
HbA1c (%)	6.9 (1.4)	6.0 (0.7)	5.6 (0.7)	<b>0.003</b>
HbA1c (mmol/mol)	51.6 (15.7)	42.4 (7.8)	37.3 (7.9)	<b>0.003</b>
Glucose (mmol/L)	7.2 (2.9)	5.5 (0.7)	4.9 (0.7)	<b>0.003</b>
Insulin (mU/L)	22.0 (8.6)	13.9 (7.4)	9.9 (6.0)	<b>&lt;0.001</b>
GIP (pg/ml)	88.4 (62.2)	85.7 (50.8)	65.9 (31.7)	0.387
GLP-1 (pmol/L)	1.0 (0.6)	1.1 (0.8)	0.7 (0.5)	0.420
Bile acids (μM/L)	9.0 (2.6)	9.8 (3.3)	9.0 (2.3)	0.654

Mean and standard deviation shown. Significant associations are highlighted in red bold.

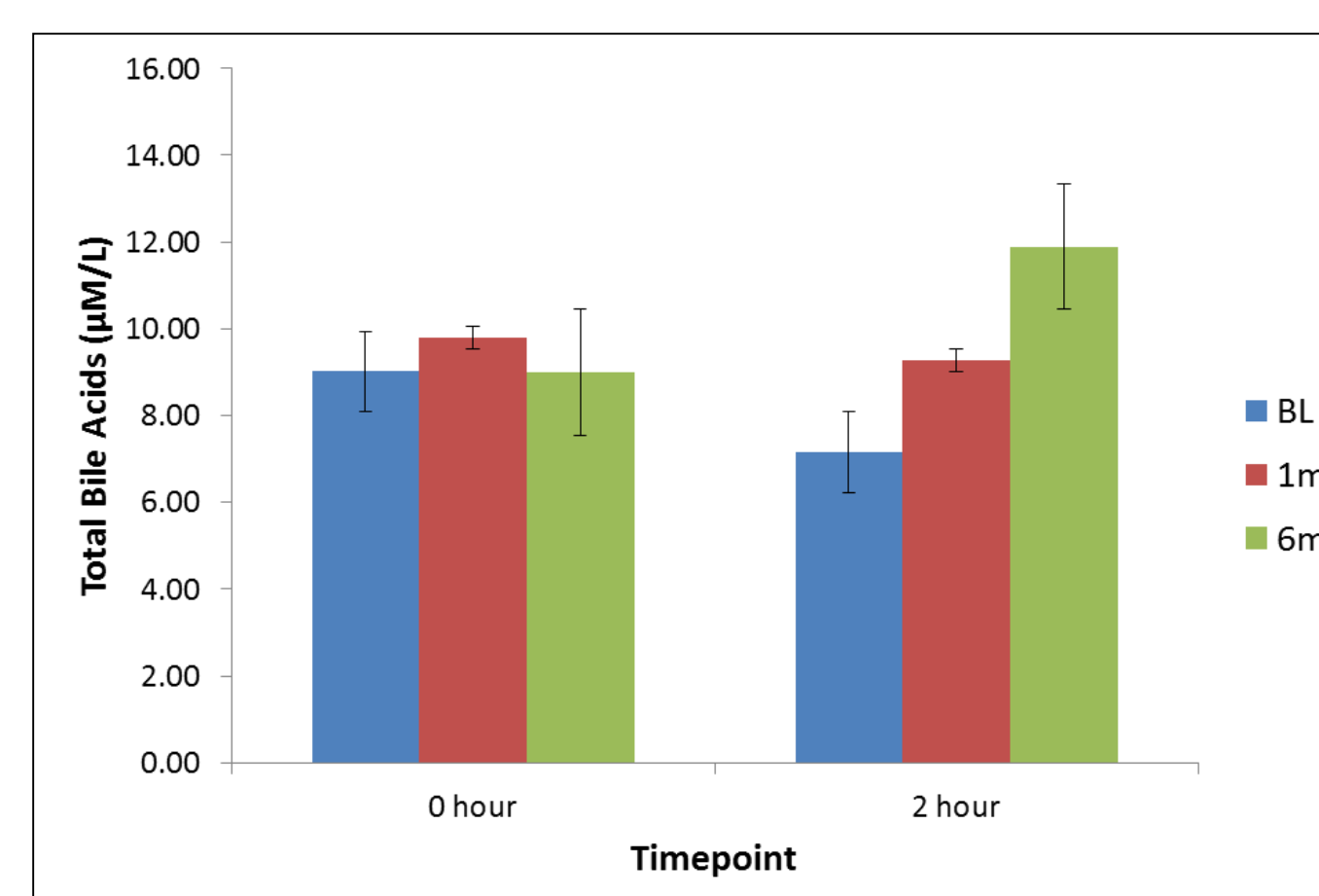


Figure 2  
Temporal changes in plasma total bile acids

- Significant increases were also observed at 2 hours at both post-operative visits when compared to baseline (BL), showing an improved post-prandial effect following surgery

BL v 1m 7.16(2.4) v 9.27(3.2)μM/L; p=0.020

BL v 6m 7.16(2.4) v 11.89(6.0)μM/L; p=0.004

- There was a significant increase in area under the curve (AUC<sub>0-120</sub>) in total bile acid at 6 months compared to baseline (p=0.017)

Figure 3  
Area under curve analysis of OGTT  
\* p=0.017; \*\* not significant

