Dynamics of Human Gut Microbiota in Response to Dietary Intervention with Potato Starch after Bariatric Surgery

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BACKGROUND

Bariatric surgery, including Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG), typically yields 50% excess weight loss.[1] Bariatric surgery alters the gut microbiome due to changes in the gastrointestinal environment, dietary modifications, and metabolism.[2] Studies show mixed impacts of bariatric surgery on the gut microbiome, some positive, such as increases in alpha diversity, others negative, including a reduction in straight short-chain fatty acids (SCFAs) levels.[3,4,5] SCFAs promote gut barrier integrity, glucose homeostasis, and appetite regulation.[6] Prebiotics, such as dietary fiber or resistant starch, are substrates fermented by the gut microbiome to produce SCFAs. Previous studies have successfully demonstrated that a resistant starch supplement can increase intestinal SCFAs in healthy populations.[7]

OBJECTIVE

Assess the impact of a 30-day resistant starch supplement - potato starch - on fecal SCFA concentrations, SCFA producing bacteria abundance, and associations between fecal SCFAs and SCFA producing bacteria, a population that recently underwent bariatric surgery.

METHODS

Study Design: Clinical trial (NCT05653648) conducted at Dartmouth Hitchcock Medical Center's (DHMC) Bariatric Surgery Program (PI: Jen Meijer), testing compliance and gastrointestinal tolerance of a 30-day dose of potato starch and assessing changes in fecal SCFA in bariatric patients from Feb 2023 – Feb 2024.

Population Characteristics: Of the 30 participants the average age was 47 years, 83% were women, 93% were of non-Hispanic ethnicity (self-reported), and 77% received a Roux-en-Y gastric bypass surgery. Fiber intake was <25 grams for 100% of the participants pre-supplementation (median: 7 grams).

SCFA Quantification: Targeted liquid chromatography/mass spectrometry.

Microbiome Characterization: Stool samples were collected using OMNIgene Gut collection kits. Samples were sequenced using 16S sequencing, processed with QIIME2, and annotated with the Silva 138 RefNR99 database.

Analysis: To compare differences in fecal SCFA concentrations and alpha diversity metrics, *t* tests were utilized. A linear discriminant analysis was performed to identify differences in genus abundance. Spearman correlations, controlling for false discovery rate, were utilized to correlate SCFA producing genera and fecal SCFA concentrations. All data analysis was performed using R version 4.0.

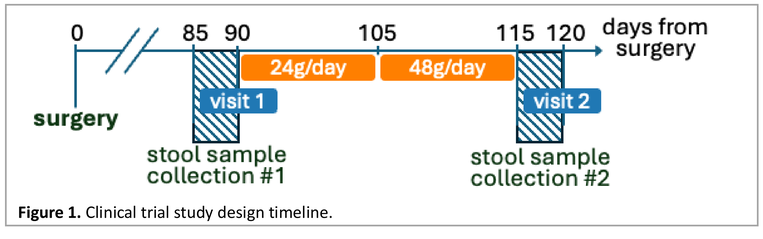

Figure 1. Clinical trial study design timeline.

RESULTS

Table 1. Changes in fecal SCFAs pre- and post-supplementation.

SCFA (nmol/mg)	Pre (n=30) median	Q1	Q3	Post (n=26) median	Q1	Q3	p-value
Acetate	46.5	34.4	59.5	51.1	35.5	65.0	0.384
Propionate	13.9	10.2	17.3	12.7	7.9	19.0	**0.048**
Butyrate	8.2	6.9	13.1	8.8	5.4	14.6	0.548
Isobutyrate	2.0	1.4	2.5	1.6	1.2	2.1	0.091
2-methylbutyrate	0.7	0.4	1.1	0.6	0.4	1.0	0.522
Valerate	2.0	1.7	3.3	1.6	1.0	2.9	0.226
Isovalerate	1.3	0.9	1.8	1.0	0.8	1.4	0.195

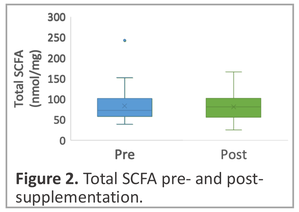

Figure 2. Total SCFA pre- and post-supplementation.

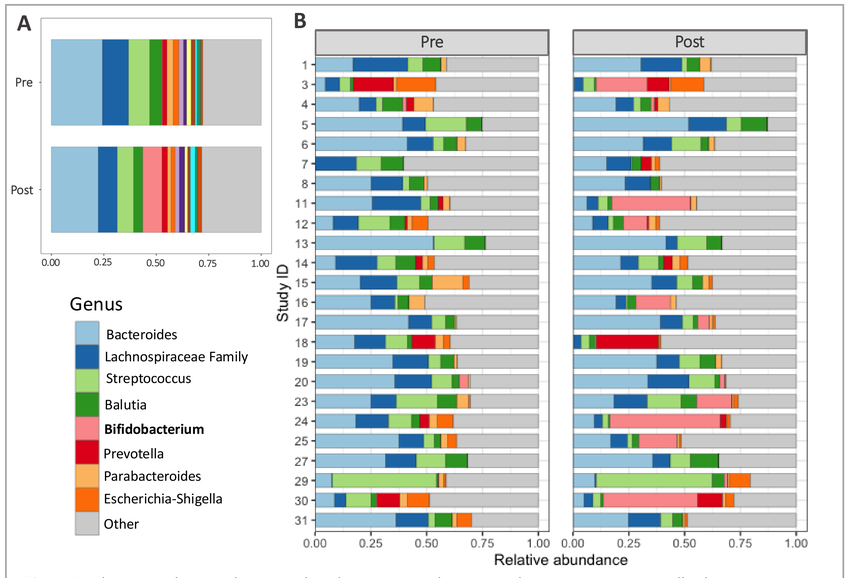

Figure 3. Changes in bacterial genera abundance pre- and post-supplementation. A. Overall relative abundance. B. Relative abundance by participant. Linear discriminant analysis identified ***Bifidobacterium*** *was* significantly enriched post supplementation ($p<0.001$). Of the 24 participants included in this analysis, 18 had an increase in *Bifidobacterium* relative abundance after supplementation.

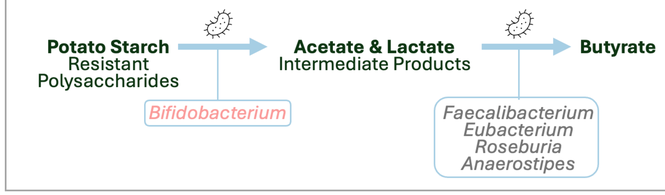

Figure 4. Butyrate production model. Proposed model of primary and secondary degrader genera. Adapted from Baxter et al.

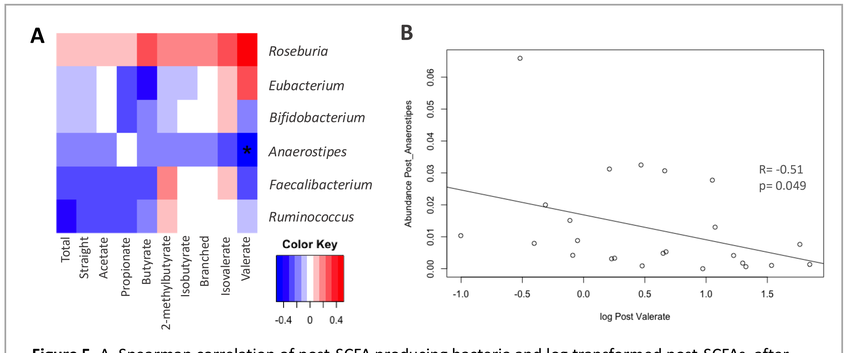

Figure 5. A. Spearman correlation of post-SCFA producing bacteria and log transformed post-SCFAs, after controlling for FDR. B. Correlation plot of valerate and *Anaerostipes* abundance after the intervention.

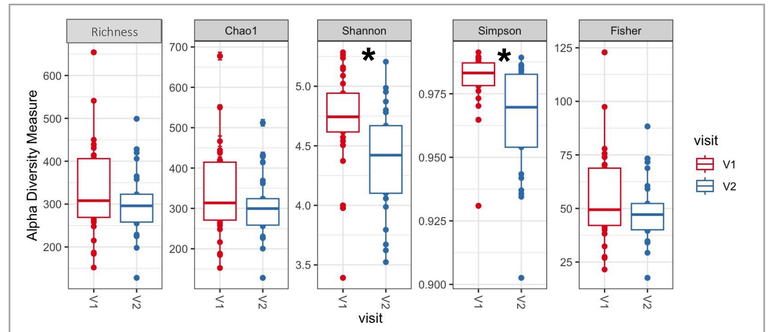

Figure 6. Alpha diversity measures. Shannon ($p=0.001$), Simpson ($p=0.003$), and Pielou's evenness ($p=0.008$) (not shown) were significantly lower (*) post-supplementation. There was no change in species richness or Faith PD.

CONCLUSIONS

Contrary to previous findings, after the potato starch supplement, propionate decreased and all other SCFAs remained unchanged (Table 1).[7] However, this project demonstrated an increase in the SCFA producing genera *Bifidobacterium* (Figure 3). These findings could be attributed to an increase in the absorption or utilization of SCFA after bariatric surgery, a phenomenon likely not occurring in previously studied healthy populations.[8] Decreases in alpha diversity are likely attributed to a decrease in taxonomic evenness, rather than the number of unique taxonomic groups (Figure 6). The observed decrease in diversity appears contradictory to expectations but is a common observation in supplementation studies.[9]

Future Directions

- Characterize SCFA producing species abundance
- Identify mechanisms underlying observed *Bifidobacterium* increases
- Develop future intervention studies in post-bariatric surgery populations with pre-surgery stool samples, a longer intervention period, a control group, and metagenomic analysis

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