Alteration of the Gut Microbiota in Gynecologic Cancer Patients with Gastrointestinal Symptoms

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Introduction

- Gynecologic cancers account for 40% of all cancer incidence and more than 30% of all cancer mortality in women worldwide
- The wide use of radiotherapy (RT) as a core modality primarily used to treat cervical and endometrial cancers has resulted in treatment-related gastrointestinal toxicities such as diarrhea and constipation
- Diarrhea and constipation are frequently reported in these cancer populations, which can profoundly impact gynecologic cancer patients' quality of life
- Growing evidence has developed to clarify the role of the gut microbiota in gastrointestinal symptoms in cancer population
- Various taxa such as *Megamonas, Novosphingobium, Prevotella*, and *Prevotella-9* have been associated with diarrhea and constipation in cancer patients
- Very limited studies evaluated the associations of the gut microbiota with gastrointestinal symptoms in gynecologic cancer patients
- The present study aimed to evaluate the gut microbiota composition in gynecologic cancer patients with gastrointestinal symptoms

Methods

- **Study Design:** Secondary data analysis
- **Participants and procedure:** 15 **w**omen with cervical and endometrial cancers were followed at pre- (T0) and 6-8 weeks post-treatment (T1)
- **Setting:** Oncology clinics at Emory affiliated hospitals and Grady Hospital, Atlanta, GA, USA
- **Inclusion Criteria:** 1) women age ≥ 18 years; 2) diagnosed with cervical or endometrial cancer who have planned curative treatment with radiation therapy (RT) or chemoradiotherapy; 3) able to read English and willing to provide informed consent
- **Exclusion Criteria:** 1) existence of co-morbidities (e.g., autoimmune diseases); 2) history of metastatic cancer; 3) current use of interferon; and 4) use of antibiotics within four weeks of the baseline session
- **Instruments:** Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)
- **Defined diarrhea and constipation:** A score ≥ 2 in PRO-CTCAE
- **Gut Microbiome:** 16S rRNA V4 region
- **Data Analysis:** The Kruskal-Wallis and PERMANOVA were used to compare α- and β-diversity between patients with and without diarrhea or constipation. The Linear discriminant analysis effect size tested taxa differences between groups. Study taxa abundance was compared to a similar study by Mitra et al., who assessed diarrhea during chemoradiation in cervical cancer patients

Results

- The patients' mean age was 52 years, 53% were Black, 52% single/divorced, 67% had cervical cancer, and 66% had stage I-II disease
- Twenty percent and 13% of the participants had diarrhea, and 47% and 36% had constipation, at T0 and T1, respectively
- β-diversity (Bray Curtis) differed between patients with and without diarrhea (p=0.05) at T1
- Patients with diarrhea exhibited a higher abundance of *Lachnospiraceae, Bilophila, Odoribacter, Lachnoclostridium, and Campylobacter* at T0 and a higher abundance of *Prevotella, Acidaminococcus*, and *Methanomassiliicoccus* at T1
- Patients with constipation had a higher abundance of *Negativicoccus, Staphylococcus, and Corynebacterium* at T0 and , exhibited a higher abundance of *Campylobacter, Intestinimonas,* and *Holdemania* at T1

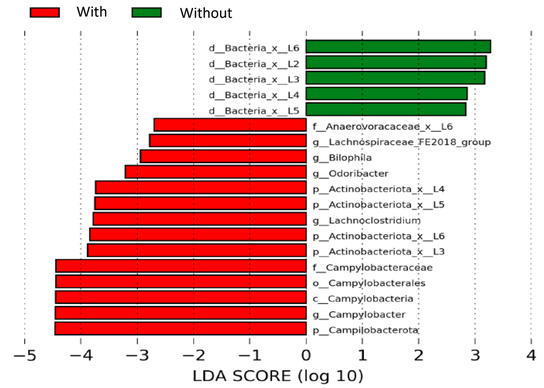

Figure 1. Taxonomic difference of gut microbiome between patients with and without diarrhea at T0

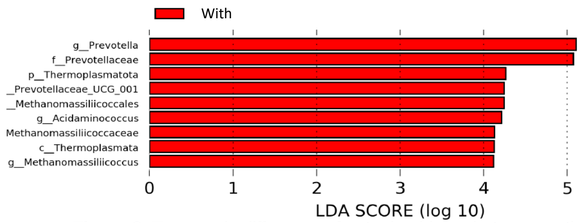

Figure 2. Taxonomic difference of gut microbiome between patients with and without diarrhea at T1

Table 1. α-diversity difference between patients with and without diarrhea

Variable	Shannon		Evenness		Faith-PD	
	H	p	H	p	H	p
T0	0.53	0.46	1.20	0.27	0.03	0.85
T1	2.70	0.10	3.33	0.06	0.13	0.71

Table 2. β-diversity difference between patients with and without diarrhea

Variable	Bray-Curtis		Jaccard		Weighted-Unifrac	
	F	p	F	p	F	p
T0	0.93	0.55	0.96	0.49	1.25	0.30
T1	1.52	0.05	0.85	0.71	1.65	0.12

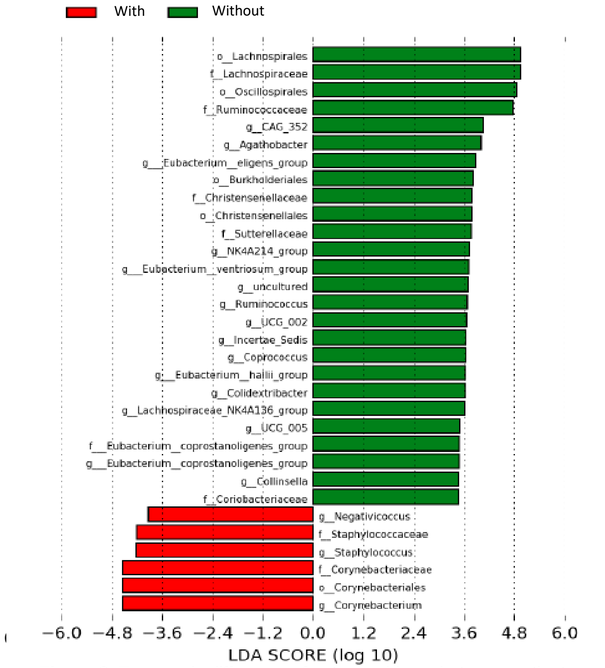

Figure 3. Taxonomic difference of gut microbiome between patients with and without constipation at T0

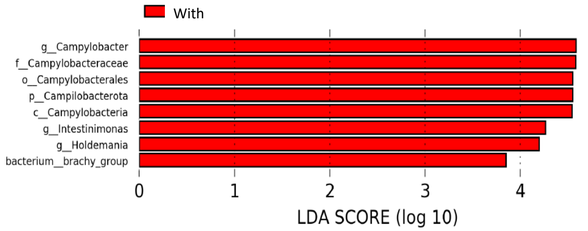

Figure 4. Taxonomic difference of gut microbiome between patients with and without constipation at T1

- Similar to Mitra et al.'s report, we found a higher abundance of *Ruminococcaceae* and *Lachnospiraceae* in patients with diarrhea

Table 3. α-diversity difference between patients with and without constipation

Variable	Shannon		Evenness		Faith-PD	
	H	p	H	p	H	p
T0	2.07	0.14	2.08	0.14	0.41	0.52
T1	0.41	0.52	0.64	0.42	0	1

Table 4. β-diversity difference between patients with and without constipation

Variable	Bray-Curtis		Jaccard		Weighted-Unifrac	
	F	p	F	p	F	p
T0	1.35	0.16	1.16	0.18	1.42	0.19
T1	0.87	0.64	0.96	0.42	0.95	0.44

Conclusion

- Significant difference in microbial taxa at various taxonomic levels from phylum to genus were observed between patients with and without diarrhea or constipation
- Significant dissimilarities among microbial communities (β-diversity) were observed between patients with and without diarrhea
- Similar taxa were observed between our data and Mitra et al.'s report
- Larger studies are required to elucidate the role of different taxa and their function in developing diarrhea and constipation to guide better treatment in women with gynecologic cancers

Reference : Mitra, A., Biegert, G. W. G.,., ... & Klopp, A. H. (2020). Microbial diversity and composition is associated with patient-reported toxicity during chemoradiation therapy for cervical cancer. *International Journal of Radiation Oncology* Biology* Physics*, *107*(1), 163-171.