

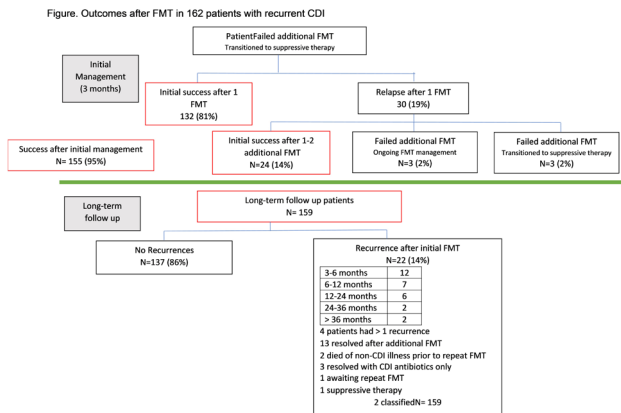
1016. Long-term Follow-up after Fecal Microbiota Transplantation via Colonoscopy or Freeze-Dried Capsules for Recurrent *Clostridioides difficile* infection

Curtis Donskey, MD¹; Michelle Hecker, MD²; Christian Rosero, MD²; ¹Cleveland VA Medical Center, Cleveland, OH; ²Metro Health Medical Center, Cleveland, OH

Session: P-57. Microbiome in Health and Disease

Background. Background: Fecal microbiota transplantation (FMT) is effective for treatment of recurrent *Clostridioides difficile* infection (CDI). However, limited data are available on the durability of FMT, especially after FMT via capsules and with more than 1 year of follow-up.

Figure. Outcomes after FMT in 162 patients with recurrent CDI



Methods. Methods: A retrospective cohort study was conducted for all patients undergoing FMT from April 2013–November 2020 in a tertiary care hospital. Initial management was considered successful if 1 to 3 FMTs resulted in improved symptoms with no diagnosis of recurrent CDI at 3 months after the initial FMT. Medical record review and telephone interviews were conducted to determine the frequency of recurrent CDI after initial successful management.

Results. Results: One-hundred sixty-two patients received 228 FMT procedures (range, 1 to 5), including 78 (34%) via colonoscopy, 144 (63%) via freeze-dried oral capsules, and 6 (3%) via nasogastric/duodenal/PEG tube. The median follow-up time after initial FMT was 61 months (range, 10 to 99 months). Initial management was successful in 132 (81%) patients after 1 FMT and in 24 (14%) patients with 1-2 additional FMTs (Figure). During long-term follow-up, 29 recurrences occurred in 22 of 159 (14%) patients evaluated. Ten (34%) of the recurrences occurred greater than 12 months after the initial FMT. Of the 22 patients with recurrence after 3 months, 16 (73%) were successfully managed with CDI therapy or additional FMT.

Conclusion. Conclusion: In our center, FMT via colonoscopy or freeze-dried capsules was very successful in initial management of recurrent CDI and 85% had a durable response with no further recurrences. However, more than 1 FMT procedure was often required to achieve initial success and to manage late recurrences.

Disclosures. All Authors: No reported disclosures

1017. Gut Microbiota Diversity and Beneficial Metabolite Production is Reduced in Liver Transplant Recipients and Associated with Post Operative Infection.

Christopher J. Lehmann, MD¹; Robert Keskey, MD¹; Matthew Odenwald, MD¹; Ravi Nayak, BS²; Maryam Khalid, BS²; Eric Littmann, BA²; Eric G. Pamer, MD;FIDSA²; Eric G. Pamer, MD;FIDSA²; Talia Baker, MD¹; ¹University of Chicago Medicine, Chicago, Illinois; ²University of Chicago, Chicago, Illinois

Duchossois Family Institute

Session: P-57. Microbiome in Health and Disease

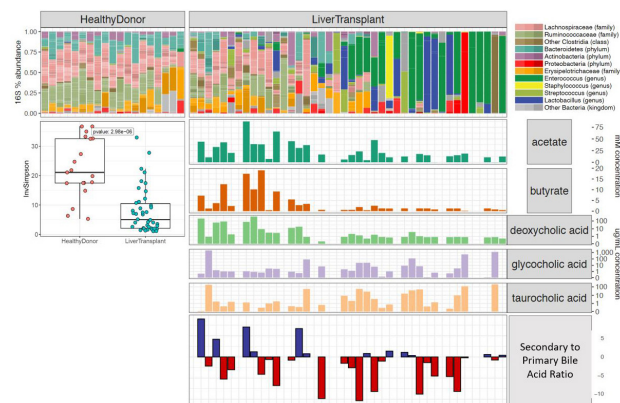
Background. Liver transplant (LT) recipients have abnormal microbiota before and after transplantation. (1,2) Associations between fecal microbiota, microbial metabolites, and clinical outcomes in liver transplantation are not well established. We correlated fecal microbiota composition and metabolite concentrations with early LT outcomes, including infection.

Methods. In a prospective observational study, we collected peri-transplant fecal samples and determined microbiota composition by 16S ribosomal RNA gene sequencing in LT recipients. Fecal short chain fatty acid (SCFA) and bile acid concentrations were measured by targeted GC- and LC-MS analyses, respectively. Inverse Simpson index was used to determine microbiota alpha-diversity in subjects and healthy controls. Clinical outcomes including length of stay, ICU admission, liver function, antibiotic use, immunosuppressive requirement and post-operative infection were correlated with microbiota composition.

Results. 69 patients were enrolled, 70 liver transplants were performed and 307 peri-transplant fecal samples were collected and analyzed. Compared to healthy controls, the fecal microbiota of LT recipients had reduced alpha-diversity ($p < 0.001$). [Fig1] Bacteroidetes, Ruminococcaceae, and Lachnospiraceae, three taxa associated with a health-promoting microbiota, and their metabolites,

SCFA and secondary bile acids, were markedly diminished 55% of LT patients. (3) Intestinal domination (>30% frequency) by Enterococcus or Proteobacteria species was common and occurred in 36% of LT recipients. 76 post-operative infections occurred in 40 LT recipients, with Enterococci causing 52% and Proteobacteria 41% of bacterial infections. In subjects with fecal samples collected within 5 days of infection, 9/17 infections were caused by the organism dominating the microbiota. [Fig2]

Microbiota Composition and Metabolite Production



16s gene sequencing color coded by taxonomy. Each bar represents one stool sample nearest to LT compared to healthy controls. Alpha diversity measured by inverse simpson index. Absolute values of microbial metabolites and ratio of primary to secondary bile acids.

Comparison of Microbiota Composition and Post Operative Infection

Patient	Infection	Organism	16s	Dominant Organism*
1	Cystitis	VRE	Enterococcus	Yes
	Colitis	<i>C diff</i>	Enterococcus, Clostridium_IV	
3	Surg Site	VRE, <i>Pseudomonas</i>	Enterococcus, Clostridium_IV, Lachnospiraceae, Streptococcus	
8	Surg Site	VRE	Enterococcus, Enterobacter	Yes
11	VAP	<i>E coli</i> , <i>Pseudomonas</i>	Moraxellaceae, Enterococcus, Prevotella	
12	Intra-Abd	VRE, <i>H parafflu</i> , <i>Prevotella</i>	Enterococcus, Enterobacter	Yes
	Intra-Abd	VRE, <i>Citrobacter</i>	Enterococcus, Enterobacter	Yes
13	VAP	ESBL <i>Enterobacter</i>	Enterobacter, Lactobacillus, Lactobacillus, Streptococcus	
38	Cystitis	VRE	Enterococcus, Clostridium_IVIII	
28	Bacteremia	<i>E coli</i>	Enterococcus, Enterobacter	
42	Surg Site	MRSA	Enterococcus, Enterobacter	
46	Intra-Abd	VRE	Enterococcus, Enterobacter	Yes
	Intra-Abd	<i>E faecalis</i>	Enterococcus, Enterobacter	Yes
49	Cystitis	ESBL <i>Klebsiella</i>	Enterococcus, Enterobacter	Yes
52	Intra-Abd	VRE, <i>E coli</i>	Enterobacter, Streptococcus, Lactobacillus, Enterococcus	Yes
	Bacteremia	VRE	Enterococcus	Yes
53	Bacteremia	<i>S epidermidis</i>	Enterococcus	

*Organism causing infection constitutes >30% abundance in microbiota

Abbreviations: VRE Vancomycin Resistant *Enterococcus*; *H parafflu* *Haemophilus parainfluenzae*; ESBL Extended Spectrum Beta-Lactamase

All bacterial infections captured with a microbiota sample within 5 days of infection.

Conclusion. Microbiota diversity and microbially derived metabolites are markedly reduced in >50% of LT recipients. Intestinal domination and post-operative infections caused by antibiotic-resistant Enterococcus and Proteobacteria correlate with loss of Bacteroidetes, Ruminococcaceae, and Lachnospiraceae species, suggesting a potential role for microbiota reconstitution therapy in LT patients.

Disclosures. Eric G. Pamer, MD;FIDSA, Nothing to disclose

1018. Bacterial Bioburden Characterization of Infected Diabetic Foot Ulcers in Hospitalized Patients in Association with Clinical Outcomes: Traditional Cultures vs. Molecular Sequencing Methods

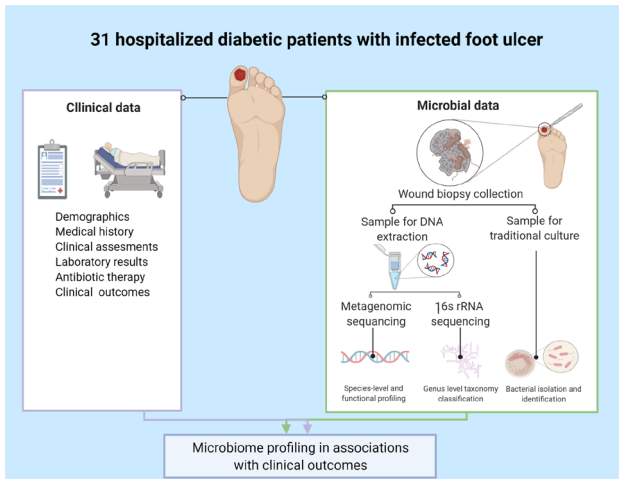
Hadar Mudrik-Zohar, MD¹; Shaqad Carasso, MSc²; Tal Gefen, PhD²; Anat Zalmanovich, MD¹; Michal Katzir, MD³; Yael Cohen, MD¹; Yossi Paitan, PhD⁴; Naama Geva-Zatorsky, PhD⁵; Michal Chowers, MD, MPH⁴; ¹Meir Medical Center, Israel, Kadima-Tzoran, HaMerkaz, Israel; ²Technion – Israel Institute of Technology, Haifa, Hefa, Israel; ³Meir Medical Center, Kfar-Saba, HaMerkaz, Israel; ⁴Meir Medical Center, Tel-Aviv University, Israel, Kfar-Saba, HaMerkaz, Israel; ⁵Technion – Israel

Session: P-57. Microbiome in Health and Disease

Background. Infected diabetic foot ulcers (IDFU) are a major complication of diabetes mellitus. These potentially limb-threatening ulcers are challenging to treat due to the impairment of wound healing in diabetic patients and the complex microbial environment characterizing these ulcers. Our aim was to analyze the microbiome of IDFU in association with clinical outcomes.

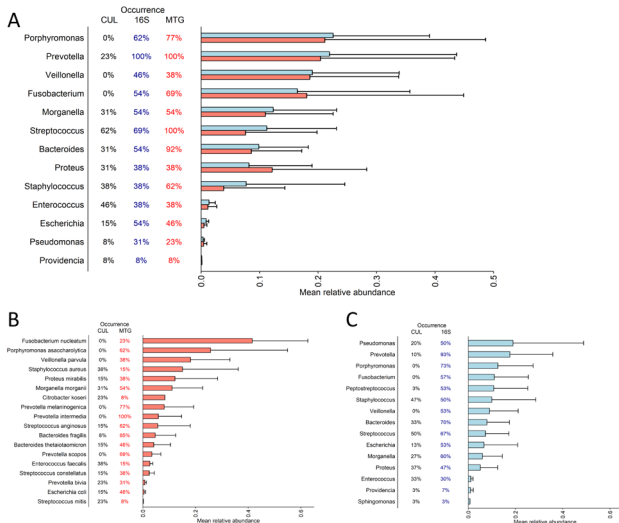
Methods. Wound biopsies from IDFU were obtained from hospitalized patients and were analyzed using traditional microbiology cultures, 16S rRNA sequencing and shotgun metagenomic sequencing. Patients' characteristics, culture-based results and sequencing data were analyzed in association with clinical outcomes.

Study Design

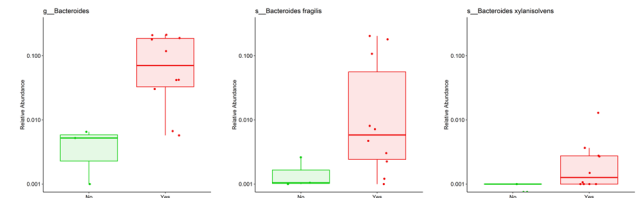


Results. 31 patients were enrolled. Significantly more anaerobic and Gram-negative bacteria were detected with sequencing methods compared to conventional cultures (59% and 76% were anaerobes according to 16SrRNA and metagenomic respectively vs. 26% in cultures, $p=0.001$, and 79%, 59% and 54% were Gram negative bacteria respectively, $p < 0.001$). Culture-based results showed that *Staphylococcus aureus* was more prevalent among patients who were conservatively treated ($p=0.048$). In metagenomic analysis the *Bacteroides* genus was more prevalent among patients who underwent toe amputation ($p < 0.001$). Analysis of metagenomic-based functional data showed that antibiotic resistance genes and genes related to biofilm production and to bacterial virulent factors were more prevalent in IDFU that resulted in toe amputation ($p < 0.001$).

Occurrences and mean relative abundances of the most prevalent bacteria of IDFU

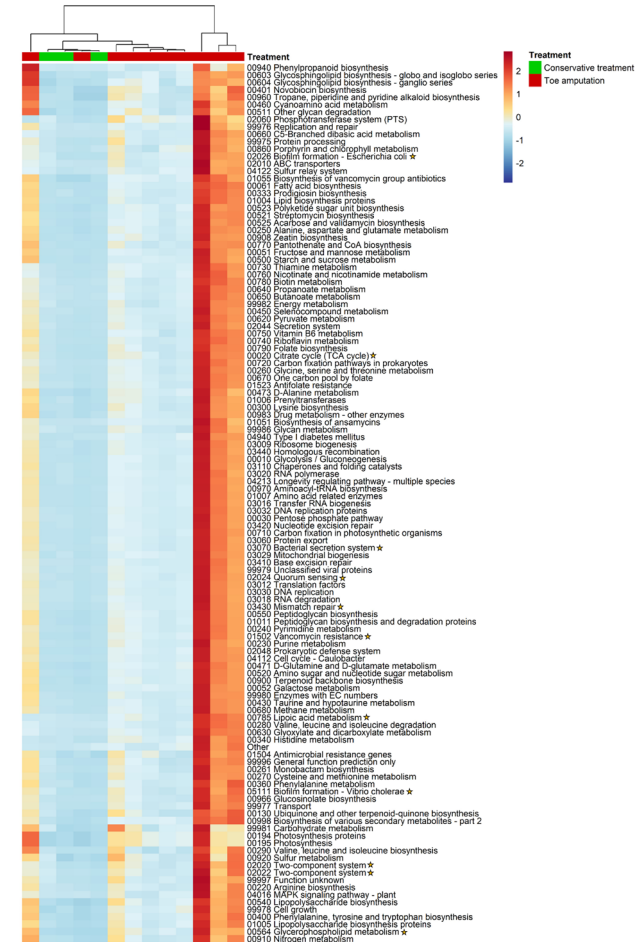


Comparison between [A] traditional cultures, 16S rRNA sequencing and metagenomic sequencing results (genera level - 12 samples) [B] traditional cultures and metagenomic sequencing results (species level - 30 samples) [C] traditional cultures and 16S rRNA sequencing results (genera level - 30 samples) CUL – cultures; 16S - 16S rRNA sequencing; MTG – metagenomic sequencing
 Bacteroides genus association with toe amputation



Bacteroides genera was more common among samples of patients who underwent toe amputation compared with samples of patients who were conservatively treated ($p < 0.001$). Species level analysis showed that *Bacteroides fragilis* and *Bacteroides xylanisolvens* predominated IDFU of patients who underwent toe amputation ($p=0.04$, $p=0.002$ respectively). No – conservative treatment; Yes – toe amputation.

Functional genes differentiating patients who underwent toe amputation from conservatively treated



Yellow stars – indicate genes that were associated with bacterial virulent factors, biofilm formation and resistant mechanisms – all were more prevalent in patients who underwent toe amputation (with p values <)

Conclusion. Molecular sequencing tools uncover the complex biodiversity of IDFU and emphasize the high prevalence of anaerobes and Gram-negative bacteria in these ulcers. Furthermore, sequencing results highlighted the possible association between certain genera, species, and bacterial functional genes to clinical outcomes

Disclosures. Yossi Paitan, PhD, Ilex Medical Ltd (Employee, Other Financial or Material Support, As of 01.01.2021 I am the Laboratories Manager of Ilex Labs)

1019. Clinical Impact of a Rapid Cerebrospinal Fluid Diagnostic Stewardship Program for Suspected Central Nervous System Infections in Children

Kevin Messacar, MD¹; Claire Palmer, MS²; Lise-Anne Gregoire, n/a²; Audrey Elliott, n/a³; Elizabeth Ackley, MD⁴; Ken Tyler, MD⁴; Samuel R. Dominguez, MD, PhD²; Samuel R. Dominguez, MD, PhD⁵; ¹University of Colorado/ Children's Hospital Colorado, Denver, Colorado; ²Children's Hospital Colorado, Aurora, Colorado; ³George Washington University, Denver, Colorado; ⁴University of Colorado, Aurora, Colorado; ⁵University of Colorado, School of Medicine, Aurora, CO