

GYNECOLOGY

Evaluation of the urinary microbiota of women with uncomplicated stress urinary incontinence



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BACKGROUND: Female urinary microbiota are associated with urgency urinary incontinence and response to medication. The urinary microbiota of women with stress urinary incontinence has not been described.

OBJECTIVE: We sought to study the cross-sectional relationships between urinary microbiota features and demographic and clinical characteristics of women undergoing stress urinary incontinence surgery.

STUDY DESIGN: Preoperative urine specimens were collected from women without urinary tract infection and were available from 197 women (174 voided, 23 catheterized) enrolled in a multicenter prospective randomized trial, the Value of Urodynamic Evaluation study. Demographic and clinical variables were obtained including stress and urgency urinary incontinence symptoms, menopausal status, and hormone use. The bacterial composition of the urine was qualitatively assessed by sequencing the bacterial 16S ribosomal RNA gene. Phylogenetic relatedness and microbial alpha diversity were compared to demographics and symptoms using generalized estimating equation models.

RESULTS: The majority of 197 urine samples (86%) had detectable bacterial DNA. Bacterial diversity was significantly associated with higher body mass index ($P = .02$); increased Medical, Epidemiologic, and Social Aspects of Aging urge index score ($P = .04$); and hormonal status ($P < .001$). No associations were detected with stress urinary incontinence symptoms. Increased diversity was also associated with a concomitant lower frequency of *Lactobacillus* in hormone-negative women.

CONCLUSION: Women undergoing stress urinary incontinence surgery have detectable urinary microbiota. This cross-sectional analysis revealed that increased diversity of the microbiota was associated with urgency urinary incontinence symptoms, hormonal status, and body mass index. In contrast, the female urinary microbiota were not associated with stress urinary incontinence symptoms.

Key words: bladder, estrogen, microbiome, stress urinary incontinence, urgency urinary incontinence

Introduction

The influence of the human microbiota on health and disease is increasingly appreciated in a variety of medical fields.¹ These microbial communities are often described by their predominant organism, the diversity of organisms within the community, and the amount of those organisms.²⁻⁴

Female urinary microbiota (FUM), composed of resident bladder bacteria, were recently recognized when bacterial DNA and low levels of live bacteria were detected in catheterized urine specimens considered “sterile” by standard urine culture.⁵⁻⁷ Enhanced urine culture techniques have provided clear evidence that FUM microbes are alive; unlike standard urine culture protocols, these enhanced culture techniques provide the

appropriate conditions for growth for a wide range of microbes.^{6,8} The living microbial community within the female bladder may provide insight into a variety of common urinary disorders, including urinary incontinence and urinary tract infections (UTI). The presence and response to urgency urinary incontinence (UUI) treatment appears related to FUM diversity and/or composition in adult women with UUI.^{2,9} There is also an association between the FUM and risk of UTI following urinary tract surgery¹⁰ or instrumentation.^{3,5} However, there is a lack of information regarding the FUM of adult women with stress urinary incontinence (SUI). The 2 most common forms of bothersome urinary incontinence (UUI and SUI) often coexist in adult women, especially those seeking surgical treatment for SUI. Information concerning the FUM has the potential to further develop the phenotype of adult women affected by urinary incontinence, with the hope of improving the targeting of treatment to improve overall outcomes.

The National Institutes of Health sponsored a large, multicenter, clinical trial of women with uncomplicated SUI planning surgery and previously established a biorepository of urine samples collected for various scientific purposes.¹¹ In this substudy, we describe the FUM analysis using 16S ribosomal RNA (rRNA) gene sequencing to characterize the cross-sectional relationships between FUM parameters and demographic and clinical characteristics of adult women undergoing surgery for SUI.

Materials and Methods

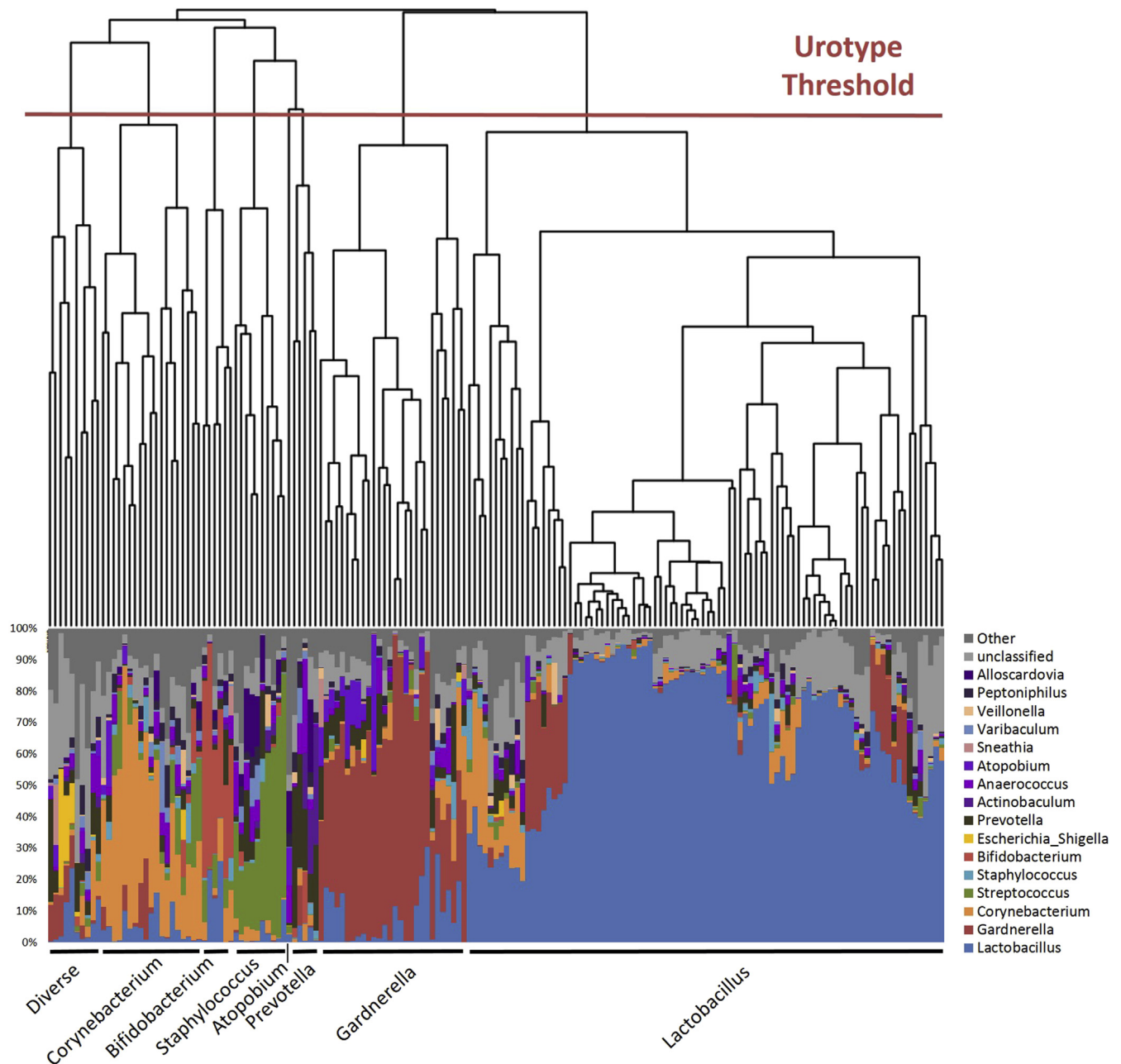
Subject recruitment and urine collection

The Value of Urodynamic Evaluation study was an institutional review board–approved, multicenter prospective randomized trial comparing surgical outcomes using 2 strategies for presurgical testing: multichannel urodynamic testing vs standardized basic office evaluation.^{11,12} Briefly, adult women were eligible if they had reported symptoms of SUI ≥ 3 months; a postvoid residual < 150 mL; a negative urinalysis/standard

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FIGURE 1
Using phylogenetic similarity to determine similar profiles (aka urotypes)



For each taxonomic level (phylum, class, order, family, genus), all samples were compared to each other using Bray-Curtis similarity, which produces a phylogenetic tree, or dendrogram, in which shorter branches link similar samples, and longer branches link more dissimilar samples. Therefore, each tree can be divided into groups or clades. When aligned to relative sequencing abundance, clades of each tree separate by identity of predominant organism. This is one example, genus classification from the first replica. Urotype indicates clades that fall into the same urotype. Each urotype is named for the predominant genus. If no one genus is predominant, then the urotype is considered nonpredominant. All corresponding graphs for each replica and each taxonomic level can be found in the [Supplementary Figure](#).

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urine culture; clinical assessment of urethral mobility; desire for SUI surgery; a positive provocative stress urinary test; and a qualifying Medical, Epidemiologic,

and Social Aspects of Aging (MESA) questionnaire^{12,13} subscale score (stress > urge). Demographic and clinical characteristics were obtained by self-

report including hormonal status, which was categorized by the study team into the hormone group that most appropriately described the patient's

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