Assesing eutopic endometrial *Fusobacterium* as an endometriosis biomarker

M.C. Graciano-España[1,2,3], K. Barnhart[4], M. Gonzalez-Monfort[1,2,3], M. Arenas-Barrero[1,2], R. S. Legro[5], T.R. Thomas[4], M. A. Rush[4], F. Vilella[1,2], M. Fernández-Sánchez[6,7], C. Simon[1,2,3,8], I. Moreno[1,2]

[1]Carlos Simon Foundation, Valencia, Spain. [2]INCLIVA Biomedical Research Institute, Valencia, Spain. [3]Pediatrics, Obstetrics and Gynecology Department, Faculty of Medicine, University of Valencia, Valencia, Spain. [4]Penn Medicine Women's Health Clinical Research Center, University of Pennsylvania, Philadelphia PA, U.S.A. [5]Penn State College of Medicine, Research, Hershey PA, U.S.A. [6]Vida Recoletas Sevilla, Seville, Spain. [7]Department of Surgery, University of Sevilla, Seville, Spain. [8]Department of Obstetrics and Gynecology, BIDMC, Harvard University, Boston MA, U.S.A.

INTRODUCTION AND OBJECTIVE

Endometriosis is a chronic inflammatory disease characterized by the presence of endometrial-like glands and stroma outside the uterus. It affects about 10% of women of reproductive age and 30-50% of those with infertility[1-4]. Recent studies have specifically implicated *Fusobacterium nucleatum* in lesion development[5]. This study aimed to evaluate the diagnostic utility of eutopic endometrial *Fusobacterium* spp. and/or *F. nucleatum* abundance as biomarkers for endometriosis and to examine its abundance across rASRM severity subgroups[6].

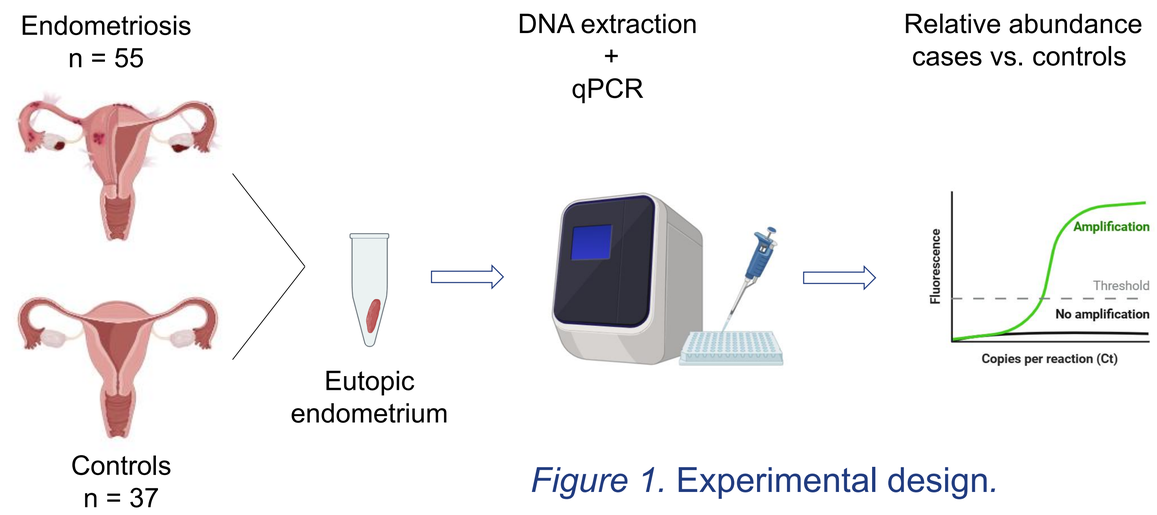

Figure 1. Experimental design.

MATERIAL AND METHODS

Design and cohort. Multicenter, retrospective case–control study (Endomarker; NCT03161704[7]).

Samples. Eutopic endometrium from 55 women diagnosed laparoscopically with endometriosis, classified as minimal-mild (MMD) (n=42) or moderate-severe disease (MSD)[6] (n=13) and from 37 controls undergoing surgery for benign conditions.

Exclusion. Women who had taken prescribed antibiotics within two months before sample collection were excluded.

Study workflow. Total DNA was extracted using the QIAamp DNA Microbiome Kit and the IndiSpin Pathogen Kit. Targeted qPCR with genus- and species-specific primers[5,8] was applied to identify *Fusobacterium* spp. and *F. nucleatum,* respectively.

Data analysis. Relative abundance was calculated with the ΔCt method considering P<0.05 as statistically significant.

RESULTS

In eutopic endometrial tissue from patients with peritoneal, ovarian, deep infiltrating, and mixed endometriosis, the relative abundance of *Fusobacterium* spp. (P=0.2582) or *F. nucleatum* (P=0.7381) did not differ significantly from that of controls (*Figure 2*).

Stratification by disease severity according to rASRM criteria also revealed no differences in the relative abundance of *Fusobacterium* spp. (P=0.1465) or *F. nucleatum* (P=0.2936) (*Figure 3*).

Consistently, no association with the presence of disease or severity of disease was identified.

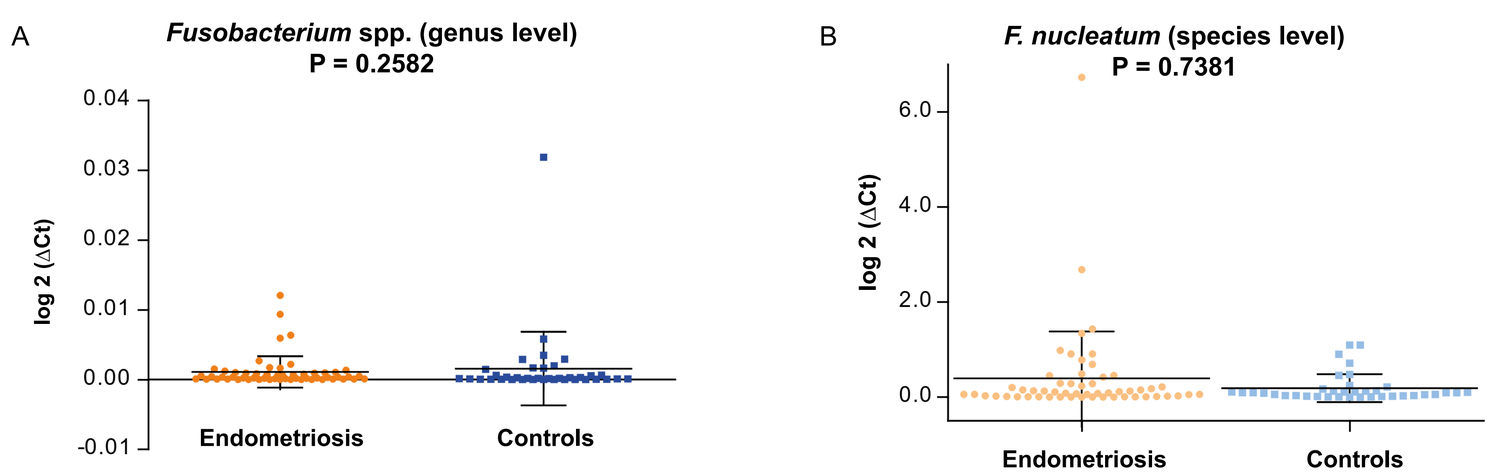

Figure 2. Boxplots comparing normalized levels of detection of *Fusobacterium* spp. (A), and *F. nucleatum* (B) in cases and controls.

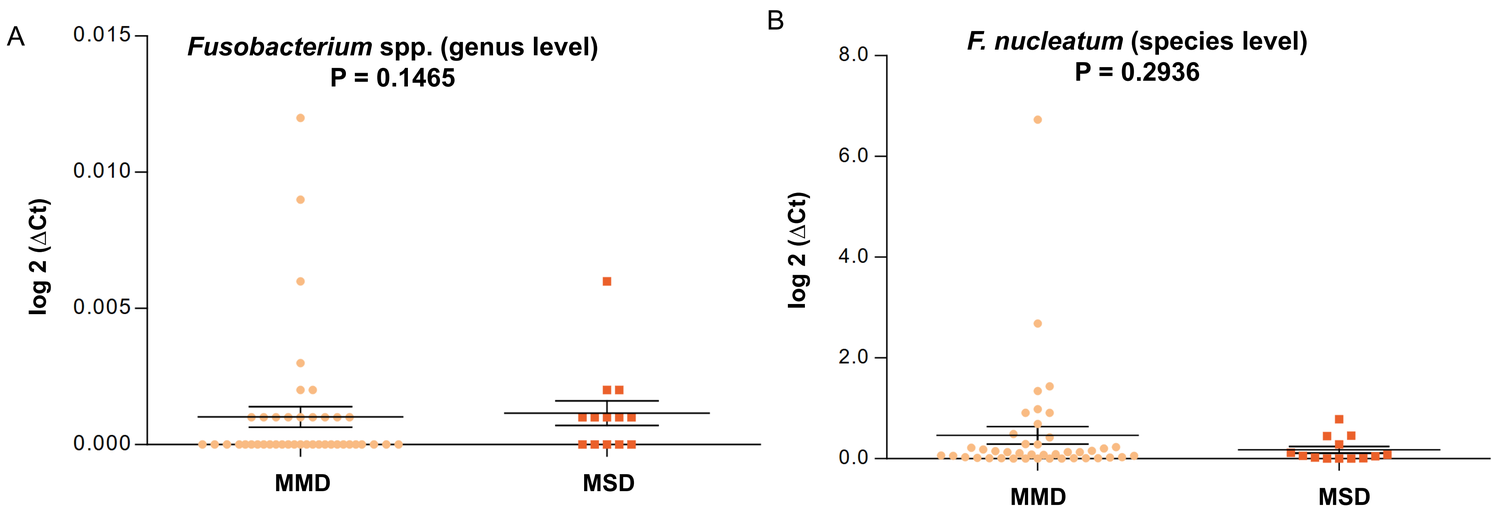

Figure 3. Boxplots representing the relative abundance of *Fusobacterium* spp. (A) and *F. nucleatum* (B) in patients with endometriosis, grouped by severity. MMD: miminal-mild: n = 42; MSD: moderate-severe: n = 13.

CONCLUSION

F. nucleatum **is not enriched in the eutopic endometria of patients with endometriosis and does not vary across rASRM severity. These findings argue against its use as a diagnostic or prognostic biomarker of endometriosis.**

In this cohort, eutopic endometrial *F. nucleatum* cannot be considered as a biomarker of endometriosis or its severity. However, this does not exclude a role of the microbiome in the pathophysiology of the disease, potentially localized to lesion microenvironments or specific subtypes.

REFERENCES

Contact information:
mgraciano@fundacioncarlossimon.com

https://rm2030.cme-congresses.com/