

Understanding endometriosis heterogeneity – sub-phenotype analysis of genetic associations (maximum 25 words)

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Study question (29/max. 28 words):

The aim of this study is to investigate whether sub-phenotype analysis of established genetic variants associated with endometriosis reveals differential mechanisms underlying surgical and symptomatic subtypes of the disease.

Summary answer (22/max. 25 words):

Preliminary results from a reduced dataset showed suggestive differential effects for genome-wide association study (GWAS) loci across surgical sub-phenotypes.

What is known already (56/max. 100 words):

Most of the known 14 genetic loci have been reported based on association with overall endometriosis, with sub-phenotypic investigations limited to ASRM stages I/II vs. III/IV. Studies using the World Endometriosis Research Foundation-Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) standardized data collection protocols now afford the investigation of these loci for detailed surgical and symptomatic phenotypes.

Study design, size, duration (32/max. 75 words):

Cross-sectional study in which genotype information from 358 women in the Oxford ENDOX study (294 cases, 64 controls) undergoing laparoscopic surgery was analysed for association with EPHect-compliant surgical and symptomatic phenotype data.

Participants/materials, setting, methods (62/max. 75 words):

Preliminary analysis of 108 endometriosis cases included 51% with endometrioma cases (not exclusive to other surgical subtypes), 68% with peritoneal disease and 31% with deep endometriosis; 40%, 14%, 19% and 27% of women were diagnosed with ASRM Stage I to IV respectively. All 14 known GWAS loci for endometriosis were tested for association with sub-phenotypes using Pearson's chi-squared and linear-by-linear association test.

Main results and the role of chance (/max. 200 words):

The GWAS locus on 2q35 (rs1250241, located in *FNI*), with genotype T/A, showed a borderline association ($p=0.035$) with peritoneal endometriosis (odds ratio (OR) of TT vs. TA=0.08, 95% confidence interval (CI): 0.01-0.78; OR of TT vs. AA=0.13, 95% CI: 0.01-1.25; OR of TA vs. AA=1.68, 95% CI:0.69-4.07), but not with endometrioma ($p=0.856$) or deep endometriosis ($p=0.307$). Analysis on additional genotype data ($n=250$) with more sub-phenotypes including infertility and pain status are underway and results will be presented at the meeting.

Limitations, reasons for caution (16/max. 50 words):

Sample size was small in the preliminary analysis, with limited power to discover a differential association pattern.

Wider implications of the findings (25/max. 50 words):

Insight into aetiological heterogeneity of endometriosis elucidated by genetics is an important avenue to ultimately develop targeted non-invasive markers of disease and novel treatment strategies.

Trial registration number:

Not applicable