Poster 7: Germline genetic testing referral and completion after diagnosis of endometrial cancer under fifty years of age

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Topic
Endometrial

Objectives
Germline pathogenic variants (PV) in Lynch Syndrome-associated genes significantly increase the risk of endometrial cancer (EC) at an early age. Starting in 2019, NCCN guidelines began to recommend germline genetic testing for EC cases diagnosed before the age of 50 to identify hereditary cancer syndromes. We assessed subsequent institutional germline genetic testing practices and findings in younger women diagnosed with EC.

Methods
The electronic medical records of a gynecologic oncology practice at a tertiary academic center were digitally searched to identify all women under 50 years old diagnosed with endometrial cancer between 2019 and 2023. Uterine sarcomas were excluded. Medical records were manually abstracted to collect data on demographics, pathology and staging (FIGO 2009 criteria), family history, genetic counseling referral and testing outcomes. Descriptive statistics were performed with comparison testing using Fisher's exact tests.

Results
136 cases of EC in individuals under the age of 50 were diagnosed and treated between 2019 and 2023, with median age of diagnosis 42 (range 16-49). At diagnosis, 66.2% (n=90) of cases were stage I-II, 33.8% (n=46) were III-IV, and 15.4% (n=21) showed mismatch repair deficiency. In total, 76 individuals (55.9%) were not referred for germline genetic testing. Two (1.5%) had prior genetic testing completed before their EC diagnosis (due to a prior cancer diagnosis), with no pathogenic variants found. Of 64 patients (47.1%) referred for genetic testing after their EC diagnosis, 50 (78.1%) ultimately underwent genetic testing with a pathogenic variant prevalence of 30% (15/50). Potentially actionable pathogenic variants were identified in 12 genes, with Lynch Syndrome-associated genes found in individuals with MMR-deficient cancer (Table 1). There were more referrals for genetic testing in those with stage III-IV disease (69.6% vs. 36.4%, $p< 0.01$), MMR-deficient cancers (76.2% vs. 42.5%, $p< 0.01$), and family history of cancer (62.3% vs. 38.5%, $p=0.008$).

Conclusions
Despite practice guidelines, genetic counseling and germline testing for endometrial cancer in women under 50 years old have not been universally implemented. This shortfall should be addressed to optimize identification of individuals with hereditary cancer syndromes.

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