A Pilot study of POLE mutations in endometrial cancer and its clinicopathological correlation with Microsatellite Instability and P53 mutations

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Abstract

Objective To determine the prevalence of Polymerase Epsilon gene (POLE) mutation, P53 mutations, and mismatch repair deficiency(dMMR) in endometrial cancer, followed by clinicopathological correlation and survival analysis Design- retrospective cohort tested prospectively and analysed for survival functions based on the findings Setting- Single institution, tertiary care centre Sample- Blocks of 48 consecutive patients with primary endometrial carcinoma were subjected to the molecular profiling Methods- Molecular classification of endometrial cancer by POLE ultramutated ,dMMR using IHC (MLH1, MH2, MSH6), and Copy number high/low (p53on IHC) was done on the preserved paraffin blocks Main Outcome Measures- prevalence of POLE mutation, P53 mutations, and deficient MMR in endometrial cancer, followed by clinicopathological correlation and survival analysis Results Eleven (22.9%) patients were dMMR , 3 (6.3%) had POLE mutation, while 2 (4.1%) had both POLE and P53 mutations (regarded as multiple classifiers). Twelve (25.0%) patients were found to have P53 mutations, while the remaining 20 (41.7%) had no specific molecular profile (NSMP). Median follow up duration was 43.5 (2-62) months with 8 recurrences and 9 deaths. Tumors with POLE mutation had the most favourable prognosis followed by the NSMP and the MMR mutated group while the P53 and multiple classifier groups had the worst prognosis in terms of OS (Log rank p : 0.006) and PFS (Log rank p : 0.001). Conclusion Integrated approach of molecular profiling should be expanded to routine testing in endometrial cancers to streamline treatment options and utilize targeted therapy such as immunotherapy Funding Institutional internal funding

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