E-poster viewing: Genetics and epidemiology

**EP169/#289**

TRENDS IN UTERINE CANCER MORTALITY IN UNITED STATES: A 50-YEAR POPULATION-BASED ANALYSIS

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**Objectives**
To analyze mortality trends in uterine cancer in the United States over 50 years.

**Methods**
Mortality data for uterine cancer from 1969–2018 were collected from the National Center for Health Statistics. Mortality rates were extracted using SEER*Stat 8.3.9. Trends (average annual percent change, AAPC) were calculated with Joinpoint 4.9.0.0. Age-adjusted mortality rate was adjusted by the US 2000 standard population. Mortality rates were adjusted by hysterectomy and pregnancy from 2001 to 2018.

**Results**
Uterine cancer mortality decreased from 1969–1997 but increased from 1997–2018. From 2001–2018, mortality rates increased across all age groups after adjusting for hysterectomy and pregnancy. Specifically in 2018, compared to younger patients (50–59 years) the mortality of older (60–69 and 70+ years) was 3x and 7x higher. Mortality rate for non-Hispanic Black (NHB) women was at least 2.2x higher than other races/ethnicities (NHB 17.6/100,000; non-Hispanic White (NHW) 7.82/100,000; Hispanic 6.54/100,000; non-Hispanic Asian/Pacific Islander 4.24/100,000). Current AAPC in NHB women shows greater annual change than some prior reports (1.87%). Intersection analysis of age and race in the over 60 age group shows NHB women had 3x higher mortality than NHW (72 vs 24/100,000). Notably, young NHB and Hispanic women (30–39 years) had a higher increase in mortality at 3.3% and 3.8% annually compared to 2.2% in NHW women.

**Conclusions**
Uterine cancer mortality has increased from 1997 to 2018. Older NHBs had the highest mortality rates, and mortality is increasing rapidly in younger minorities. Further studies of molecular, social, and environmental factors are needed to explain and reduce these trends and disparities.

**EP170/#317**

FACILITATED CASCADE TESTING FOR FAMILIES WITH IDENTIFIED MUTATIONS ASSOCIATED WITH HEREDITARY GYNECOLOGIC CANCERS

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**Objectives**
We evaluated the feasibility of a facilitated referral pathway for cascade genetic testing (GT) for patients with mutations associated with gynecologic cancers.

**Methods**
This is a prospective cohort study of patients with BRCA1, BRCA2, BRIPI, MSH2, MLH1, MSH6, PMS2, EPACAM, RAD51C, and RAD51D mutations from March 2019-March 2022. Eligible patients were offered a facilitated referral pathway for GT for first and second-degree relatives (figure 1). Decision Regret Scale and Impact of Events Scale assessed psychological impact at 3-months. The primary outcome was the proportion of patients with a relative who successfully completed GT.

**Results**
Of 583 eligible patients, 73 (13%) enrolled in our study. Reasons for declining participation were: no eligible relatives or previously tested (235, 40%), lost to follow-up...
BESIDE BREAST/OVARIAN MALIGNANCY: OTHER CANCER RISK PROFILE IN BRCA1 AND BRCA2 PATHOGENIC VARIANTS

EP171/#1044

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Objectives The clinical significance of genetic testing of BRCA1 and BRCA2 Pathogenic Variants (PV) in women with breast and ovarian cancers is widely recognized. However, there is paucity of evidence to include other cancer types in clinical management guidelines. We aim to study the prevalence of different types of cancers in BRCA 1 AND BRCA2 PV carriers and to associate those with the mutation type.

Methods This is a cross-sectional study of women carriers of BRCA1 and BRCA2 PV, who attended our designated carrier clinic in a tertiary medical center We compared cancer incidence among the three most prevalence PVs in Israel: 185del, 6174del and 5382insc.

Results A total of 2,230 women were included. BRCA1 mutation comprised 62.6% of the cohort, BRCA2 36.6% and 0.8% were carriers of both genes. Breast and ovarian/fallopian tube/peritoneal cancer was prevalent in 106 women(4.7%). Most prevalent other cancers were: cutaneous, 1.1%, colon, endometrial and cervical –0.6% each and thyroidal and pancreatic cancers, 0.4% each. The risk of any cancer was higher in 5382insc than 6174del and 185 del; 54.8% vs. 46.3% vs. 36.0% respectively, p<0.001. When excluding breast and ovarian/fallopian tube/peritoneal cancer, the risk of other cancer was similar among the three mutations: 9.3% in 5382insc, 7.2% in 6174del and 7.3% in 185del, (p=0.521).

Conclusions The results of this large-scale study suggest that pathogenic variants in BRCA1 and BRCA2 were associated with non-negligible risk of other cancers. This risk seems not to be associated with the type of mutation, however larger studies are warranted.

INTEGRATED MOLECULAR PROFILE OF PLATINUM RESISTANT EPITHELIAL OVARIAN CARCINOMA

EP172/#350

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Objectives Epithelial ovarian carcinoma (EOC) is a serious malignancy with high mortality due to late diagnosis and drug resistance development. Drug resistance is one of the major obstacles to successful anticancer therapy. The main aim of our study was to analyze molecular profile based on gene expression, DNA methylation level, and genetic variability in EOC patients stratified by the platinum therapy resistance status.

Methods For the present study, we selected 72 EOC patients with sensitive (N=43) or resistant (N=30) status. Whole genome expression of protein-coding genes was profiled by mRNA sequencing technology (N=60), IncRNA expression by whole transcriptome RNA sequencing (N=23), global methylation by DNA microarrays (N=50), and somatic mutation rate by whole exome sequencing (N=50).

Results Molecular profile of platinum resistant EOC patients differed from sensitive EOC patients in upregulation of five protein-coding genes (NEURL1, FCGBP, MMP11, NCAM1, and ARMC3) and five IncRNA (ADAMTS9-AS1, TCF21-AS1, ARMC3-AS1, LINC-HIST2H3P52-35, and LINC-BCR-4), higher methylation of seven protein-coding genes (ABCC4, ABCB10, SLC1A7, SLC19A2, SLC50A1, XPC, and FOXO1) and three IncRNA (LINC00263, LINC00460, NEAT1) and higher frequency of mutations in TP53 gene. On the other hand, three protein-coding genes (LPL, CD36, FABP4), and three IncRNA (LINC-IGGL5, LINC-TMEM121-12, CHST6-AS1) were downregulated, lower methylation was observed for ATP1A1 gene, and the Hippo pathway genes were less mutated in resistant patients.

Conclusions Our study shows a complex network of dysregulated genes and gene expression products connected with the resistance status of EOC patients which should be further characterized. Supported by INTER-ACTION LTAUSA19032, GACR no. 21–140825, AZV no. NU20–09–00174 and GAUK no.1074120.