GI Gap in Genetic Testing for Inherited Susceptibility to Colorectal Cancer

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INTRODUCTION

- Hereditary cancer syndromes are estimated to account for ~5–10% of all cancer diagnoses.
- Population prevalence estimates of Lynch Syndrome nearly match those of Hereditary Breast and Ovarian Cancer (HBOC) (1:440 vs. 1:400).
- Genetic testing is believed to be underutilized for indication of Gastrointestinal Cancer Syndromes (GICS) as compared to HBOC.
- **Hypothesis #1: Genetic testing is quantifiably underutilized for GICS.**
- **Hypothesis#2: Multiplex gene panel (MGP) testing identifies actionable mutations, enabling improved patient care.**

METHODS

- We conducted a multicenter prospective cohort study of patients undergoing cancer-risk assessment using a 25 multi-gene panel (MGP).
- Gene Panel: *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53.*
- Eligibility criteria were the following; 1) not previously tested 2) age ≥ 18 3) ≥ 2.5% probability of mutation (by model or clinical index of suspicion) 4) written informed consent.
- Patients were recruited from August 2014 to June 2015 at Los Angeles County Medical Center, USC Norris Comprehensive Cancer Center, and Stanford Cancer Institute.

RESULTS

Figure 1: GI GAP in New Cancer Diagnosis vs Genetic Testing

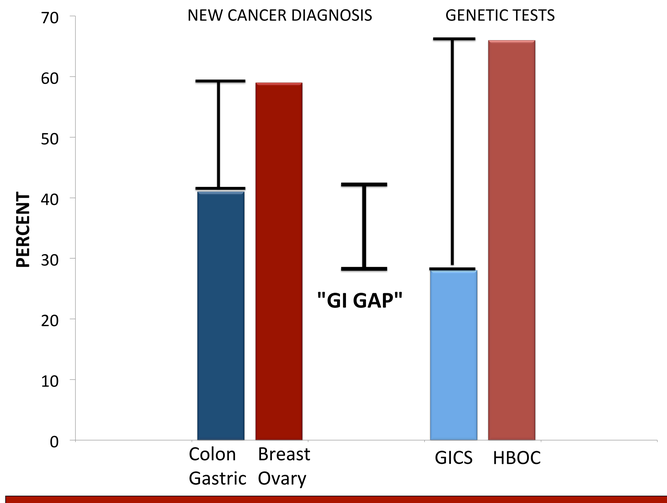


Figure 2: "GI GAP" per Institution

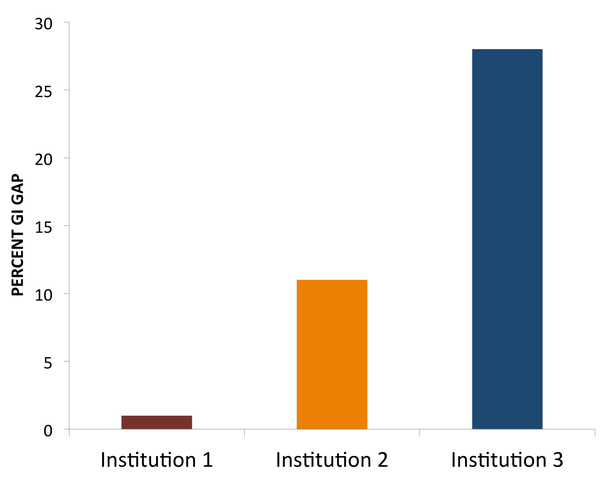


Figure 3: Mutation Detection Results

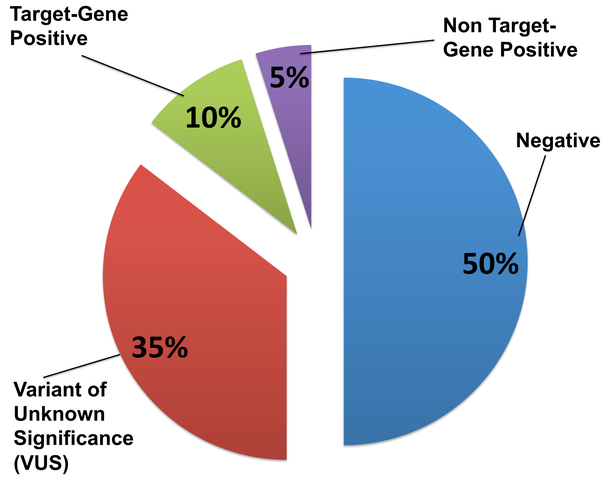
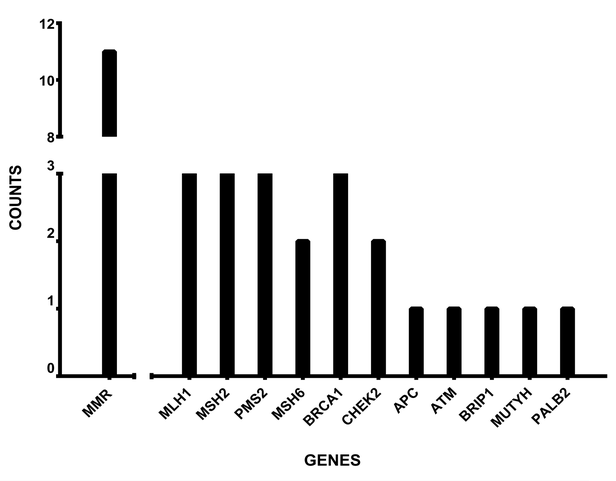


Figure 4. Deleterious Mutations Identified in GICS Cohort



RESULTS

- Newly diagnosed colorectal (CRC) and gastric cancer (GC) constitute 42% of the 1,798 new diagnoses of all, CRC, GC, breast, and ovarian cancers at the three participating centers, using cancer registry data. (Figure 1)
- Among 500 tested individuals, 29% were for primary evaluation of GICS (n=144) as compared to 66% (n=332) tested due to a primary evaluation of HBOC. (Figure 1)
- Genetic testing is underutilized for GICS by an average of 13%. The specific "GI Gap" at 3 different institutions was 1%, 11%, and 28%. (Figures 1 and 2)
- Beyond traditionally tested genes (*APC, CDH1, MLH1, MSH2, MSH6, PMS2*, and *MUTYH*), 7 patients (4.9%: 95% CI, 2.4%-9.7%) had an off-target DM. (Figures 3 and 4)
- Results were clinically meaningful, as one patient with an unexpected DM in BRCA1 was subsequently found to have ovarian cancer.

CONCLUSIONS

- Genetic testing for GI cancer syndromes is underutilized by approximately 13%, in comparison to testing for HBOC. Multiplex gene testing offers high-yield recognition of both on-target cancer syndromes (10%) and off-target mutations (5%) and has clinically meaningful outcomes.
- This study demonstrates the need for increased awareness and utilization of genetic testing for detection of cancer syndromes, especially among gastroenterologists.

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