Title:

Increasing Uptake of Hereditary Cancer Multi-gene Panel Testing: Overcoming Initial Barriers

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Description:

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BACKGROUND:

Multigene panels (MGP) testing genes associated with multiple cancer syndromes became commercially available in March 2012, presenting healthcare providers with a new way to order genetic testing for hereditary cancer susceptibility. Initial wariness towards MGP was felt by both genetic counselors and physicians across a variety of subspecialties. Concerns were raised regarding higher rates of variants of uncertain significance (VUS), the lack of established management and testing guidelines for some genes, increased turnaround times (TAT) and uncertainty regarding how to counsel patients for broad spectrum panels. However, since 2012, numerous studies have been published demonstrating increased

diagnostic yield offered by MGP and atypical phenotypes observed in patients with mutations in previously well-defined syndromic genes such as *TP53* and *CDH1*, and data sharing between laboratories is improving VUS interpretation. This study aimed to explore whether initial concerns about MGP have been tempered by analyzing the utilization of MGP over a three-year period at a clinical diagnostic laboratory.

METHODS:

Quarterly ordering trends for *BRCA1/2* and Lynch syndrome (LS) single-syndrome tests were compared to MGP; grouped into 'focused MGP' containing only higher penetrance genes, and cancer site-specific or pan-cancer 'expanded MGP' comprised of high- and moderate-penetrance genes. Hereditary breast and ovarian cancer (HBOC) tests (all tests containing *BRCA1/2*) were analyzed from July 2013-September 2015. LS tests (all tests containing LS genes) were analyzed from April 2012-September 2015. Ordering provider (OP) specialties were annotated as surgery, oncology, obstetrics & gynecology/primary care, gastroenterology, and gynecologic oncology, and genetics provider (geneticist, genetic counselor, advance practice nurse, or other clinician with genetics training) involvement, or lack thereof, was also noted. Statistical analysis was performed using the Fisher's exact test.

RESULTS:

Comparison of combined HBOC and LS tests in the third quarter (Q3) 2013 versus Q3 2015 revealed that expanded MGP significantly increased in frequency from 39% to 65% ($p<0.01$). Conversely, single-syndrome tests significantly decreased in frequency from 37% to 18% of HBOC tests ($p<0.01$). In fact, in 2015, all MGP have consistently accounted for >80% of all HBOC tests compared to <65% in 2013. Similar trends were observed for LS tests, with MGP comprising 66% of tests in Q2 2012 and LS single-syndrome tests accounting for the remaining 34%, while in Q3 2015 MGP accounted for >90% of all tests encompassing LS genes. Regarding OP specialty, analyses of HBOC and LS tests across five OP specialties revealed that all MGP have been utilized more frequently across all specialties in 2015 compared to 2013. Genetics provider involvement also significantly increased the utilization of expanded MGP across all specialties ($p<0.01$).

CONCLUSIONS:

Consistent with recent literature, results from this study demonstrate markedly increased utilization of MGP compared to 2012 when initially available. In addition, genetics provider uptake of MGP is consistently greater than non-genetics provider uptake. Despite the observed decrease in single-syndrome and focused MGP tests, these tests still account for 34% of total tests in Q3 2015, thus supporting clinicians' desires for tiered testing options. While additional research is needed to directly investigate OP attitudes towards MGP, explore OP rationale for ordering single-syndrome, focused MGP, or expanded MGP testing, and assess reasons for differences among genetics providers versus non-genetics providers, the increased utilization of MGP observed in this study supports the idea that initial concerns surrounding MGP have lessened over time.

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Genetic Testing
NextGen Sequencing

Primary Topic Focus:
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