EVALUATING THE PERSONAL AND FAMILY HISTORY OVERLAP BETWEEN HEREDITARY CANCER SYNDROMES

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BACKGROUND

- Current NCCN guidelines for hereditary cancer genetic testing are divided among different cancer site guidelines.
- Guidelines for colorectal cancer screening cover several hereditary colon cancer syndromes (Lynch syndrome (LS), FAP, MFAP, Peutz-Jeghers, and Juvenile Polyposis) while guidelines for hereditary breast cancer testing include Hereditary Breast and Ovarian Cancer (HBOC), Li Fraumeni and Cowden syndromes.
- The premise underlying this system is that hereditary cancer syndromes have distinct cancer profiles.
- However, overlapping cancers among these syndromes make it difficult to identify which diagnosis is most appropriate for a given patient.
- To quantify the overlap among hereditary cancer syndromes, we reviewed personal and family history of patients in a genetic testing population.
- We also analyzed results from hereditary cancer panel testing to assess the potential benefit of this technology for patients with overlapping cancer phenotypes.

METHODS

- We analyzed personal and family histories submitted with genetic testing for Lynch syndrome or HBOC to identify patients who met testing criteria for both syndromes at a commercial laboratory.
- Tests for a specific family mutation, the common Ashkenazi Jewish HBOC mutation or a single LS gene were excluded.
- We also examined the commercial testing results of a 25 gene hereditary cancer panel to identify patients who were tested due to the clinical presentation of one syndrome but had a mutation associated with the other syndrome.

RESULTS

- Of patients tested for HBOC, 70% had family histories that met 2012 NCCN criteria for LS.
  - Of the HBOC patients that overlapped with LS guidelines, 89.3% qualified based on family history, 9.5% qualified based on personal history alone, and 1.2% qualified based on a combination of personal and family cancer history.
- Of patients tested for LS, 29.5% met criteria for HBOC.
  - Of LS patients that also met HBOC guidelines, 56.6% qualified based on family history alone, 18.1% qualified based on personal cancer history alone, and 25.2% qualified based on a combination of personal and family history.

CONCLUSIONS

- This analysis suggests that genetic testing strategies that focus on a single hereditary cancer syndrome may miss patients with genetic syndromes due to complicated cancer histories.
- Advancements in sequencing technology, including hereditary cancer panels, will allow patients to receive the appropriate diagnosis and will require new guidelines to be set as this technology becomes part of the standard of care.