PS3-03-26: Guideline concordant surgical management of hereditary variants of uncertain significance: Outcomes from a safety-net hospital

K. P. Verma[1], L. J. Oshry[1], M. Rudderman[1], I. Arshad[2], B. Moy[3], L. Wu[1]

[1]Department of Medicine, Section of Hematology and Oncology, Boston Medical Center, Boston, MA, [2]Boston University School of Public Health, Boston, MA, [3]Department of Medicine, Division of Hematology and Oncology, Massachusetts General Hospital, Boston, MA

Background

- Germline genetic testing can identify pathogenic variants (PV) that meaningfully guide cancer screening and management
- Variants of uncertain significance (VUS) create clinical challenges, as guidelines advise that they should not be used to direct cancer management or risk-reducing surgical decisions
- Studies show gaps between evidence-based guidelines and clinical practice regarding hereditary breast and ovarian cancer (HBOC) VUS management
- To improve access to high quality cancer genetics care, the multidisciplinary High Risk Cancer Genetics Clinic (HRC) was launched at Boston Medical Center (BMC) in May 2023



Objectives

To describe patterns of surgical management for patients with VUS in HBOC genes before and after the establishment of the HRC at BMC, a major safety-net hospital in the Northeast

Methods

Retrospective analysis of patients with HBOC gene VUS, comparing surgical management in the two years before vs after HRC establishment

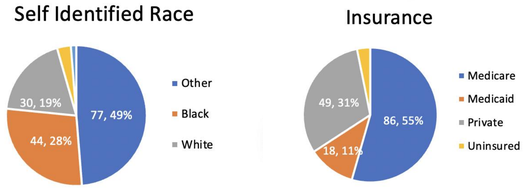
Inclusion: Patients with family history or personal diagnosis of cancer who underwent germline genetic testing and had VUS in BRCA1, BRCA2, BRIP1, TP53, PALB2, PTEN, CDH1, STK11, RAD51C, or RAD51D. (n = 438)

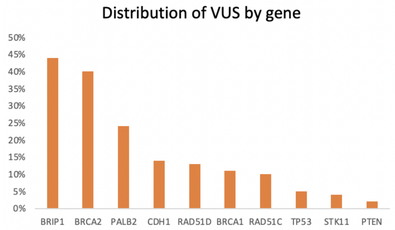
Exclusion: Males, metastatic disease, germline PV in HBOC (n = 280)

Before HRC: n = 64 patients

After HRC: n = 94 patients

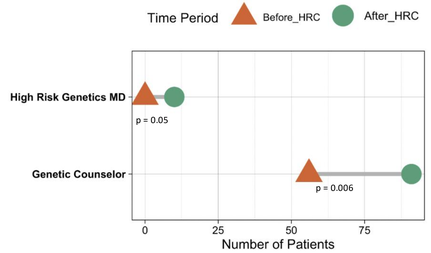
Results





Results

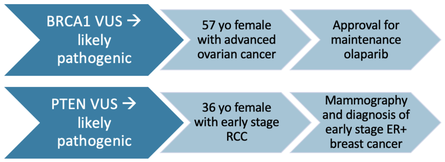
Establishment of the High-Risk Clinic was associated with an increase in both genetic counselor and High-Risk genetics MD visits



There were no cases of prophylactic bilateral mastectomy among patients without breast cancer nor bilateral salpingo-oophorectomy among those without ovarian cancer

Patients with HBOC VUS	Before HRC	After HRC	P-value
Non-breast cancer patients who underwent bilateral mastectomy (BLMa)	0/45	0/62	-
Non-ovarian cancer patients who underwent bilateral salpingo-oophorectomy	0/64	0/90	-
Breast cancer patients who underwent BLMa	1/19 (5.3%)	4/32 (12.5%)	0.64

Reclassification of VUS to likely PV resulted in one patient who appropriately initiated olaparib and a second patient who was found to have early stage breast cancer after high-risk screening



Discussion

- Institutions may vary in germline genetic testing practices. To optimize care, it is essential to evaluate approaches to germline testing, result interpretation, and the influences of these practices on decision-making
- At our safety-net hospital, surgical management of patients with HBOC VUS remained guideline concordant
- No patients underwent risk reducing mastectomies based solely on an HBOC VUS
- Following the integration of HRC, we observed meaningful improvements in genetics-related care:
  - Increased access to genetic counselors and high risk genetics physicians
  - Timely re-evaluation of VUS classifications
  - Prompt clinical action when a VUS was reclassified to PV

Future Directions

- Future efforts should prioritize expanding access to germline testing, increasing cascade testing, and ensuring guideline concordant management for individuals with PV
- Because VUS are frequently observed in non-European ancestry populations while most reclassification data still derive from European ancestry cohorts, addressing disparities in genomics requires greater representation of minority populations in research and databases
- We should examine how clinicians communicate VUS reclassification to PV, and whether management and outcomes differ when results are conveyed by genetic counselors and HRC providers compared with other clinicians

Contact

Karina P. Verma, MD
Boston University/Boston Medical Center
Email: karina.verma@bmc.org

References

1. Núñez Jr O, Nunez G, Wolde TM, Heath R, Donenberg TR, Silva-Smith R, Jeanjean MB, Moore JF, Crystal JS, Kesmodel S, Rojas KE. *Variant of uncertain significance (VUS) genetic testing results and mastectomy choice in lumpectomy-eligible patients.* J Clin Oncol. 2024;42(16_suppl):10601.
2. Brehany S, Colton M, Duarte C, Baliton M, McCranie AS, Okuyama S. Hereditary Cancer Screening and Outcomes at an Urban Safety-Net Hospital. JCO Precis Oncol. 2024 Jun;8:e2300699. doi: 10.1200/PO.23.00699.
3. NCCN Guidelines 2025, Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate.
4. Manahan ER, Kuerer HM, Sebastian M, Hughes KS, Boughey JC, Euhus DM, Boolbol SK, Taylor WA. Consensus Guidelines on Genetic Testing for Hereditary Breast Cancer from the American Society of Breast Surgeons. Ann Surg Oncol. 2019 Oct;26(10):3025-3031. doi: 10.1245/s10434-019-07549-8. Epub 2019 Jul 24

This presentation is the intellectual property of the author/presenter. Contact them at karina.verma@bmc.org for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com