Impact of Multigene Panel Testing on Medical Management: Preliminary results of a pre- and post-test clinician survey

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Identification of individuals with germline variants in cancer predisposition genes has risk management and therapeutic implications. Adoption of multi-gene panel testing (MGPT) has led to the development of management guidelines for numerous high and moderate risk breast/ovarian cancer genes. Limited data exist on the impact of MGPT results as they pertain to these guidelines. Here we describe the results of a survey designed to assess the effect MGPT has on clinical decision making.

Clinicians were invited to participate in an IRB-approved study using a web-based survey tool to assess clinical management recommendations before and after MGPT. Pre-test survey invitations were emailed to clinicians upon submission of each order. A post-test survey link was emailed to those who completed a pre-test survey upon results disclosure. For this analysis, we examined responses for cases in which at least one breast cancer susceptibility gene was tested. Genes were grouped into three categories: **H**igh **R**isk breast cancer genes with breast **G**uidelines (abbreviated HRG: *BRCA1, BRCA2, CDH1, TP53*), **M**oderate **R**isk breast cancer genes with breast **G**uidelines (MRG: *ATM, CHEK2, NBN, NF1, PALB2*), and genes often found on breast cancer gene panels but that have **N**o breast **G**uidelines (NG: *BARD1, BRIP1, FANCC, RAD51C, RAD51D*). Concordance to National Comprehensive Cancer Network (NCCN) v1.2019 guidelines was calculated with regards to recommendations for mammogram, breast MRI, risk reducing mastectomy (RRM), and bilateral salpingo-oophorectomy (BSO).

Pre- and post-test surveys were completed by 160 unique providers for 792 cases. Cases with positive or inconclusive findings in genes outside of the HRG, MRG, or NG groups and those with an elevated polygenic risk score (n=127) were excluded from this study. Of the 665 remaining cases, 90 patients had positive (13.5%), 106 had inconclusive (15.9%), and 469 had negative results (70.5%). At least one management change was recommended in most individuals with positive results in HRG or MRG genes (77.3%), in contrast to those with inconclusive (8.5%) or negative results (8.1%). The proportion of patients with at least one recommended management change did not significantly differ between individuals with positive findings in HRG and MRG genes (82.9% vs. 73.5%, p=0.31). In the HRG group, recommendations were mostly concordant with guidelines for mammogram (85.2%), MRI (74.1%), RRM (82.8%), and BSO (85.7%). Recommendations in the MRG group were also mostly concordant with guidelines for mammogram (93.0%) and MRI (81.4%). No individuals in the NG group received a change in mammogram or MRI recommendations based on test results. Seven of 51 females with positive findings in genes without RRM recommendation were advised to consider RRM (13.7%), and two of 47 females with positive findings in genes without BSO recommendation were advised to consider BSO (4.3%). Recommendations to enroll in a clinical trial were made in 15.5% of all positive cases.

The data from this ongoing study demonstrate that positive genetic test results frequently lead to changes in medical management recommendations and in some cases therapeutic options. Our observation that positive results in high risk and moderate risk genes lead to an adjustment in management at similar rates demonstrate the benefit of MGPT. Further, most respondents adhere to NCCN guidelines, even without considering clinical factors and contraindications not captured by this survey that contribute to patient management. While these findings support the clinical utility of MGPT, continued study is essential to guide clinicians and payers on the impact MGPT has on medical management and ultimately health outcomes of high-risk individuals.