The Patient Experience in a Prospective Trial of Multiplex Gene Panel Testing for Cancer Risk

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Abstract

Background: Multiplex gene sequencing panels (MGP) are increasingly used for assessment of hereditary breast cancer risk. Compared to testing for BRCA1 and BRCA2 (BRCA1/2) only, testing more genes increases the likelihood of identifying a deleterious mutation (DM) and/or a variant of uncertain significance (VUS), which might cause distress, uncertainty or regret about testing. Little is known about the patient experience of MGP testing.

Methods: We conducted a prospective study of MGP testing, using a panel of 25 genes: *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11,* and *TP53*. Participants were enrolled at three medical centers and were eligible if they met standard genetic testing guidelines or if they had a ≥2.5% probability of a DM in any gene on the panel, as calculated by predictive models (e.g. IBIS, Penn II, MMRPro). Participants were surveyed about their experiences with MGP testing including distress and uncertainty at baseline (before test results disclosure) and three months later. The 25-item Multidimensional Impact of Cancer Risk Assessment (MICRA) scale measured distress, uncertainty and positive experiences at three months after testing. We present a planned interim analysis after enrolling 500 of 2000 total participants.

Results: Of 500 participants, 332 (66%) were referred for suspicion of hereditary breast/ovarian cancer syndrome. Of these 332, 97% were female, 79% were white, 43% were Hispanic and 33% were Spanish-speaking only; for 25%, high school was their highest level of education. A total of 48% had breast cancer, 5% had ovarian cancer, and 7% had another cancer: 11% had a DM and 35% had VUS in one or more genes. At study entry most participants thought about cancer rarely or not at all (69%, 95% confidence interval (CI) 58%-77%), and few (7%, CI 3%-14%) had thoughts of cancer that affected their daily lives; results were unchanged three months later, after genetic results disclosure (Chi-squared test, p-value >0.1). MICRA scores at three months were low for distress (mean score 2 out of a possible 30) and uncertainty (mean score 7 out of 45), and high for positive testing experiences (mean score 9 out of 15). Most (82%, CI 72%-88%) participants wanted to know all of their MGP results even if the clinical relevance was not fully understood, and most (87%, CI 79%-93%) never regretted learning their MGP results.

Conclusions: Among diverse participants of a prospective, multi-center MGP testing trial, cancer- and genetic testing-related distress were low at entry and remained low three months later. These results provide no evidence for an increase in distress or uncertainty after MGP. Longer-term follow-up in a larger cohort is underway.

Background

- Multiplex gene panel (MGP) use is increasing
- 15-40 genes instead of only 2 (*BRCA1/2*)
- Increases detection of mutations by 5%-15%
- Results are complex: more genes = more variants of uncertain significance (VUS)
- ***Does MGP testing cause patients distress?***

Methods

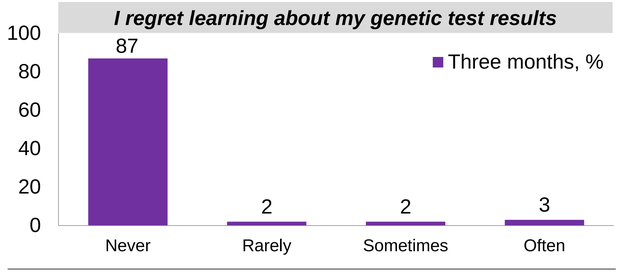
- Prospective cohort study of MGP; goal N=2000
- 25-Gene Panel: *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53*
- Eligibility criteria: 1) no prior genetic testing; 2) age ≥18; 3) ≥2.5% mutation probability by risk models
- Recruited 2014-2015 at 3 centers (LA County, USC, Stanford); interim analysis n=500, 332 breast cancer history
- Surveys on testing experiences at entry and 3 months after testing (longer follow-up underway)
- Multidimensional Impact of Cancer Risk Assessment (MICRA) scale of distress, uncertainty, positive experiences

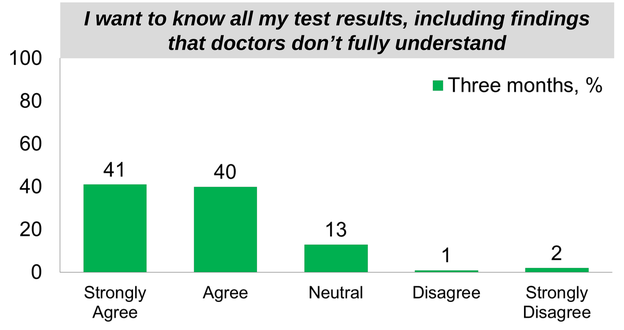
Results

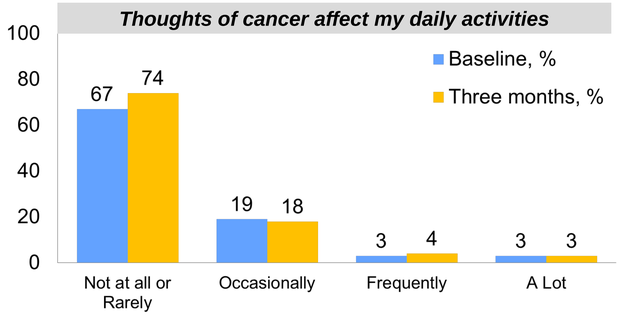
Participant Characteristics (N = 332)

Gender	Female (n, %)	321, 97%
Age	Median Age (years, range)	50 (range 19-92)
Race	White	265, 80%
	Black	14, 4%
	Asian	35, 11%
	Mixed/Other	18, 5%
	Hispanic Ethnicity	143 , 43%
Language	English-Speaking	168, 51%
	Spanish-Speaking Only	110, 33%
	Mandarin-Speaking Only	7, 2%
Education	High School or Less	109, 33%
	Some College	64, 19%
	College Graduate	72, 22%
	Graduate School	50, 15%
Cancer History	No Personal Cancer History	133, 40%
	Breast Cancer	160, 48%
	Other Cancer (ovary, skin, pancreas, colon)	39, 12%

Results







- **Test results**: 53% negative, 36% VUS, 11% positive
- **Survey completion to date:** Baseline 86%; 3-month 27%

Conclusions

- Diverse (43% Hispanic, 33%≦high school)
- **Early results not suggestive of distress**
- 87% never regretted learning about results
- 81% wanted all their genetic test results
- No increase in intrusive thoughts (p>0.5)
- MICRA results low for distress, uncertainty

Limitations

- Incomplete study sample (goal: N=2000)
- Limited follow-up time (goal:≧12 months)

Next Steps

- Complete study accrual and follow-up
- Track clinical outcomes (changes in care):
  - Screening interventions
  - Preventive interventions
- Assess correlation with genetic test results
- Multivariable analysis of survey results

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