Preventive Surgery after Multiplex Genetic Panel Testing (MGPT)

Gregory E. Idos, MD, MS[1,2]; Allison W. Kurian, MD, MSc[3]; Charite Ricker, MS[1,2]; Duveen Sturgeon, MSN[1]; Julie O. Culver, MS[1]; Kerry E. Kingham, MS[3]; Rachel Koff, MS[3]; Nicolette M. Chun, MS[3]; Courtney Rowe-Teeter, MS[3]; Peter Levonian, MS[3]; Christine Hong, MS[1]; Meredith A. Mills, BA[3]; Cindy S. Ma, BS[3]; Johnathan M. Lancaster, MD, PhD[4]; Krystal Brown, PhD[4]; John Kidd, MS[4]; Kevin J. McDonnell, MD, PhD[1]; Uri Ladabaum, MD, MS[3]; James M. Ford, MD[3]; Stephen B. Gruber, MD, PhD,MPH[1,2]

1. University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA 2. Keck School of Medicine, University of Southern California, Los Angeles, CA 3. Stanford Cancer Institute, Stanford University School of Medicine, Stanford CA 4. Myriad Genetics Inc, Salt Lake City, UT

BACKGROUND

- Guidelines recommend consideration of prophylactic surgery for patients with a germline pathogenic variant in some cancer predisposition genes.
- We assessed surgical utilization (mastectomy, oophorectomy, and hysterectomy) in a prospective, multi-institutional cohort study of MGPT.

METHODS

COHORT AND FOLLOW-UP

- 2,000 patients were recruited between July 2014 and November 2016 at 3 medical centers: USC Norris, LA County, and Stanford.
- Patients were enrolled if they met standard clinical criteria for genetic testing or were predicted to have a ≥ 2.5% probability of inherited cancer susceptibility using validated prediction models.
- All patients had testing with a 25- or 28-gene MGPT.
- Patients completed questionnaires at 3, 6, and 12 months after genetic results disclosure.

ANALYSIS

- Patients were included if they did not have sugery prior to MGPT and responded to questions pertaining to surgery utilization (N=1,537). Patients were excluded if they left this section of the questionnaire blank.
- Surgery utilization was assessed according to the following:
  - Patient-reported indication for surgery (treatment or prevention)
  - Cancer history (personal history of a relevant cancer; Figure 1)
  - MGPT test results [Positive, pathogenic variant (PV); VUS, variant of uncertain significance; Negative, benign variants]
  - Gene-specific cancer risk and surgery recommendations (Figure 1)

Figure 1. Relevant cancers and genes by surgical intervention

Genes Associated with Relevant Cancer	Mastectomy	Oophorectomy	Hysterectomy
Relevant Cancer	Breast	Ovarian	Uterine/Endometrial
With Surgical Recommendations (Guidelines)	***BRCA1, BRCA2, TP53, PTEN, CDH1***	***BRCA1, BRCA2, BRIP1, RAD51C, RAD51D, MLH1, MSH2, EPCAM***	***MLH1, MSH2, MSH6, PMS2, EPCAM, PTEN***
Insufficient evidence for preventive surgery (consider)	*ATM, CHEK2, PALB2, BARD1, NBN, STK11*	*MSH6*, PMS2*, STK11* *Based on ACG Guidelines	*STK11*

RESULTS

Table 1. Patient characteristics

Surgery	All Enrolled (N=2,000)	Reported Surgery (N=195)
Age (Years)		
Median (Range)	51 (16, 92)	48 (27, 77)
Gender, N (%)		
Female	1,614 (80.7)	194 (99.5)
Male	386 (19.3)	1 (0.5)
Ethnicity, N (%)		
Hispanic/Latino	813 (40.7)	107 (54.9)
Non-Hispanic/ Latino	1,182 (59.1)	87 (44.6)
Unknown	5 (0.3)	1 (0.5)
Personal Cancer History, N (%)		
Affected	1,451 (72.6)	183 (93.8)
Unaffected	549 (27.4)	12 (6.2)

- Overall, 12.7% (195/1,537) of patients reported surgery after MGPT (median follow-up 13 months; Table 1).
  - Only 31.8% (62/195) of patients specified that their surgery was preventive (Figure 1).
- Preventive surgery utilization was significantly higher among patients who tested Positive compared to those testing Negative (p<0.001) or VUS (p<0.001).
  - Positive: 15.5% (30/194) had preventive surgery
  - VUS: 2.4% (12/505) had preventive surgery
  - Negative: 2.4% (20/838) had preventive surgery
- Among PV positive patients, preventive surgery was almost exclusively utilized by those with PVs in genes with surgery recommendations or associated with the relevant cancer (Table 2).
- Preventive surgery was very low among patients testing Negative or VUS who had no personal history of cancer in the relevant organ (Figure 1).
  - Preventive surgery use in this patient group was often based on relevant family history (Figure 2).

Figure 2. Surgery utilization. Denominators given for each category are the number of patients with the indicated cancer history and MGPT result. Patients who indicated that their surgery was for prevention are shown in yellow.

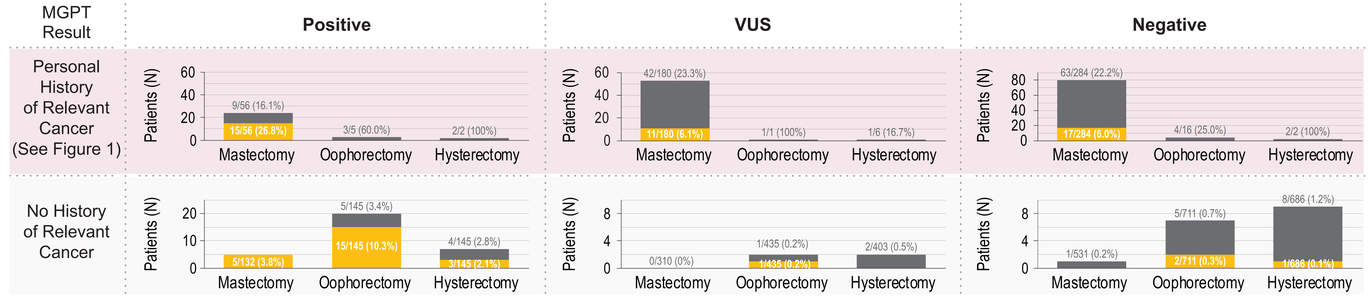
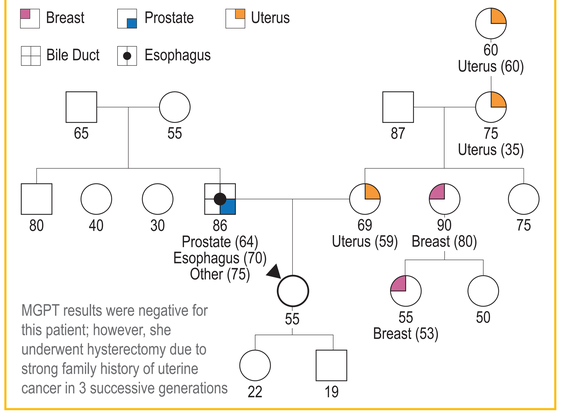


Table 2. Gene distribution and surgery utilization in patients with Positive MGPT results

Gene	Personal History of Relevant Cancer (See Figure 1) N*	Surgery, Prevention N (%)	Surgery, Treatment N (%)	No History of Relevant Cancer N*	Surgery, Prevention N (%)	Surgery, Treatment N (%)
Mastectomy						
Genes with Mastectomy Recommendation (See Figure 1)	27	9 (33.3)	5 (18.5)	34	3 (8.8)	0
Other Breast Cancer Risk Genes (See Figure 1)	12	5 (41.7)	2 (16.7)	23	2 (8.7)	0
Non-Breast Cancer Risk Genes	17	1 (5.9)	2 (11.8)	75	0	0
Oophorectomy						
Genes with Oophorectomy Recommendation (See Figure 1)	4	0	3 (75.0)	61	14 (23.0)	4 (6.6)
Other Ovarian Cancer Risk Genes (See Figure 1)	0	0	0	11	0	0
Non-Ovarian Cancer Risk Genes	1	0	0	73	1 (1.4)	1 (1.4)
Hysterectomy						
Genes with Hysterectomy Recommendation (See Figure 1)	1	0	1 (100)	24	1 (4.2)	0
Non-Uterine/Endometrial Cancer Risk Genes	1	0	1 (100)	121	2 (1.7)	4 (3.3)

*The number of patients who completed the survey questions pertaining to each type of surgery. Total N varies by surgery.

Figure 3. Surgery utilization with a negative MGPT result



CONCLUSIONS

- Prophylactic surgery was not over-utilized by patients undergoing MGPT after one year of follow-up.
- VUS findings did not lead to inapprorpaite medical utilization.

Please contact Greg Idos at Gregory.Idos@med.usc.edu with any questions

Presented at ASCO on June 3, 2018