STAT Reasons and Ordering Outcomes for Hereditary Breast Cancer Genetic Testing

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Objective: When indicated based on personal and family history, women facing a diagnosis of breast cancer often undergo hereditary cancer genetic testing. Turnaround times for genetic testing range from seven days to four weeks and vary based on genes analyzed, technology, and laboratory workflow. Genetic testing is processed "STAT" when deemed necessary by the ordering clinician. For these cases, the laboratory uses extra resources to expedite testing, as identification of a pathogenic mutation may directly impact the patient's management plan. For example, a woman with a positive genetic test result may choose to undergo prophylactic mastectomy rather than lumpectomy in order to reduce the risk for another breast cancer primary. We evaluated a cohort of STAT hereditary cancer test orders to determine indications for these requests and potential outcomes of the results.

Methods: Test request forms for 1,137 breast-related STAT orders from April-June of 2015 were reviewed. Information about personal diagnosis, reason for STAT request, test performed, and genetic test results was gathered.

Results: The majority of breast-related STAT requests (n=701; 61.6%) were for multigene panel tests (MGPT). The remaining orders were for *BRCA1/2*-only (n=264; 23.2%), *BRCA1/*2 with reflex to a MGPT (n= 165; 14.5%), and non-*BRCA1/2* single-gene tests (n=7; 0.6%). Most probands had invasive breast cancer or DCIS at the time of testing (n=1,120; 98.5%) and the remainder (n=17; 1.5%) had a past history of breast cancer or a non-malignant breast lesion. Upcoming surgery was indicated as the reason for the majority of STAT orders (n=1079; 94.8%), whereas non-surgical treatment decisions such as chemotherapy or clinical trials were indicated less frequently (n=33; 2.9%).

Overall, 119 (10.5%) mutation-positive probands were identified; 73 of whom harbored mutations in genes that would warrant consideration of bilateral prophylactic mastectomies as per current NCCN guidelines, including *BRCA1* (n=31), *BRCA2* (n=36), *PTEN* (n=1), and *TP53* (n=5). Additionally, NCCN guidelines contraindicate radiation therapy for individuals carrying germline *TP53* mutations. The remaining 46 probands carried mutations in genes for which no breast surgical NCCN guidelines exist (*APC, ATM, BARD1, BRIP1, CHEK2, MLH1, MUTYH, NBN, PALB2, PMS2,* and *RAD51C*).

Conclusion: Most probands undergoing STAT testing were pending breast cancer surgery. Surgical decisions were potentially impacted by positive test results for at least 6.4% of patients, and many individuals who had negative test results likely elected breast conserving surgery. STAT orders may not have been urgent in 1.5% of cases since these patients were not pending treatment. STAT testing requires extra resources and should be utilized only when timing is critical; however, it can be essential in guiding medical management for patients facing immediate treatment decisions.