Genetic Risk and Compliance with Risk Reduction in a High-Risk Breast Population

Amy Pratt, DO[1], Lauren Cournoyer, BS[2], Beverly Hay, MD[3], Kathryn Edmiston, MD[1], Madhavi Toke, MD[1], Anne Larkin, MD[2], Jennifer LaFemina, MD[2]

University of Massachusetts, Departments of [1]Medicine, [2]Surgery, and [3]Pediatrics; Worcester, MA

INTRODUCTION

While national guidelines exist regarding the role of genetic testing, surveillance, and risk-reducing therapies in women at increased risk of breast cancer, prior reports note that only about 50% of these patients proceed with genetic testing and that pathogenic mutations are identified approximately 10% of the time. Data regarding compliance with subsequent recommendations, though, is strikingly sparse.

OBJECTIVES

The aim of this study is to assess the incidence of pathogenic mutations associated with breast cancer as well as the compliance with recommendations for screening and risk-reducing therapy within the context of a high-risk breast population.

METHODS

A retrospective analysis of subjects evaluated due to an increased risk of breast cancer was conducted from January 2013-August 2016. Variables including genetic testing recommendations and results as well as compliance with recommendations for clinical follow-up, radiologic screening, prophylactic surgery, and risk-reducing medication were assessed. The study schema is summarized in Figure 1.

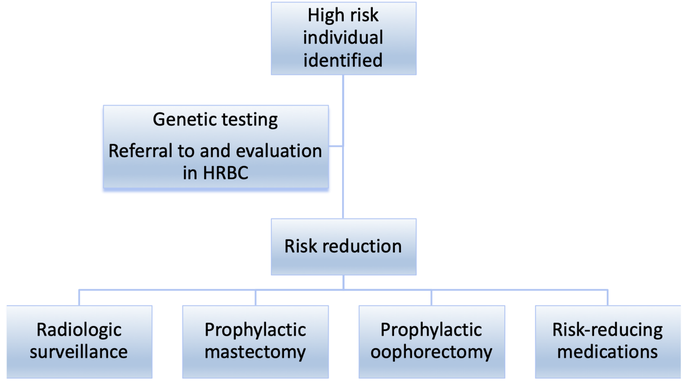

Figure 1. Study schema

RESULTS

1491 patients were evaluated. 58% (n=866) underwent genetic testing: 43% (n=89) due to personal history, 38% (n=79) due to family history, and 19% (n=41) due to both family and personal history (Fig. 2). 24% (n=209) of those tested (14% of all subjects) were found to have a genetic mutation; 16% of those tested harbored pathogenic mutations associated with breast cancer. The most common deleterious mutations were *BRCA1* (n=47; 22%), *BRCA2* (n=32; 15%), *MSH6* (n=16; 7%), *MLH1* (n=10; 5%), *APC* and *MUTYH* (n=5 each; 2%), *TP53* (n=4; 2%), and *CHEK2* and *MSH2* (n=3 each; 1%) (Fig. 3). Variants of uncertain significance (VUS) were identified in 33% of tests (n=72). 32% (n=67) of subjects were lost to follow-up.

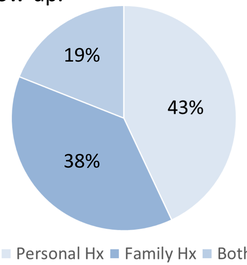

Figure 2. Indication for genetic testing of those who underwent testing (n=866)

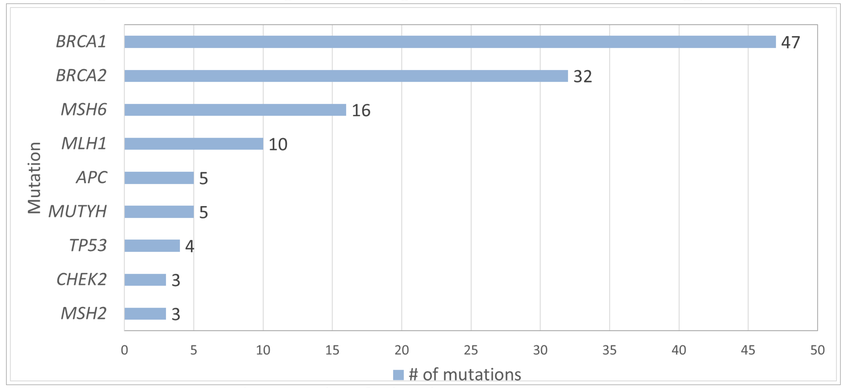

Figure 3. Identified pathogenic mutations

After excluding those lost to follow-up, 93% (n=126/136; denominator for analysis indicates those who received such a recommendation) complied with recommendations for clinical follow-up, 88% (n=88/100) complied with radiologic surveillance, 88% (n=52/59) complied with prophylactic mastectomy, 73% (n=52/71) complied with prophylactic oophorectomy, and 95% (n=41/43) complied with risk-reducing medication (Fig. 4).

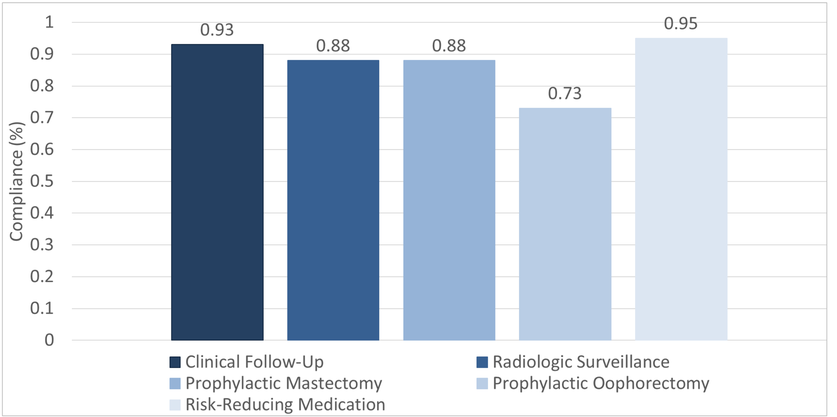

Figure 4. Compliance (%) with recommended interventions

CONCLUSIONS

This analysis is one of the largest reports to date regarding compliance with recommendations within the context of a high-risk breast population. Data demonstrate that nearly 60% of subjects seen for an increased risk of breast cancer underwent genetic testing, yielding an appropriate 16% incidence of newly diagnosed pathogenic mutations associated with breast cancer. *BRCA1* and *BRCA2* were most common; VUS were identified in 1/3 of cases. While nearly a third of subjects were lost to follow-up, those who did follow-up demonstrated significant compliance with recommendations for screening and risk-reduction. Further work is needed to identify barriers to compliance in this population and to provide insight into the outcomes associated with long-term compliance with screening and risk-reducing therapy recommendations.