

# Genetic Mutation Carriers: A Growing, Evolving, and Unique Breast Surgery Population

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## Abstract

As science advances, more genetic variations and mutations are uncovered offering greater insight into which patients are predisposed to increased risk for development of breast cancer. A reasonable option for these patients includes bilateral prophylactic mastectomy with reconstruction. However, this cohort of patients is unique from the average breast cancer patient in that they are typically younger and may have distinct objectives for their surgical outcomes. This paper aims to better understand this unique and expanding population, as well as their expectations for surgical outcomes both aesthetically and oncologically. We discuss how oncologic and plastic surgeons may collaborate to navigate this area and effectively provide cutting-edge and novel surgical treatments, such as nipple sparing mastectomy and prepectoral single stage reconstruction. Furthermore, we examine the role of social media in this distinct population, with patient to patient virtual information sharing and how this may impact patient referrals in a manner diverging from traditional hospital-based patterns.

**Key Words:** Genetic Mutation; Prophylactic Bilateral Mastectomy; Reconstruction

## Introduction

Surgeons today are adapting to an era of technology where patients are empowered like never before. Medical websites like WebMD are allowing patients to identify their own symptoms and diagnoses, requiring doctors to grapple with the positive and negative consequences associated with the influence of the web. Patients are also connected through social media and online groups where they can support each other, and share information regarding their treatment and management. Patients have the power to investigate, rate and review their physicians and surgeons through online platforms, the results of which can have significant implications in the practice of physicians. All of this influx of information guides and complicates the healthcare decisions of the modern patient. This is increasingly true for the breast cancer patient population.

Armed with the internet, breast cancer patients are increasingly aware of potential outcomes, both oncologic and aesthetic. The era of patients being grateful simply for surgery to cure their cancer is disappearing. With an ever-evolving understanding of risk and prevention via the discovery of additional genetic mutations that confer risk for breast cancer, care for this patient population has become increasingly complex, with decisions regarding Bilateral Prophylactic Mastectomy (BPM) being forced onto a younger generation of patients. In addition, awareness from prominent public figures and known mutation carriers

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such as Angelina Jolie has drawn admirers and critics alike for their decision to undergo BPM and reconstruction in the absence of cancer; surgeons must now adapt to a younger generation of patients with an elevated consciousness. A surgeon today must not only be constantly on top of the literature associated with breast cancer care, they must also adapt to patients who seek out their surgeons via less traditional methods. Online reviews, Facebook groups and virtual patient to patient interactions, which were once reserved for identifying high quality eating establishments, are now being used to distinguish high quality surgeons from a menu of practitioners.

The aim is to better elucidate the Genetic Mutation Carrier (GMC) female patient interested in risk reduction surgery and reconstruction and their unique characteristics, with an additional focus on how a surgeon can navigate the associated enhanced expectations. We will discuss aesthetic and oncologic considerations of BPM and reconstruction, as well as optimal collaboration between the surgical oncologist and plastic surgeon needed to provide cutting-edge surgical treatment and novel surgical treatments such as prepectoral (above the muscle) and direct to implant (single stage) reconstruction. Finally, we will examine the role of social media for patient-to-patient virtual experience sharing and our personal experience with referral practices in this distinct population.

### **Genetic Mutation Carriers - An Emerging Population of Breast Surgery Patients**

GMCs are an emerging population of patients with unique characteristics, perspective, and expectations of surgery. Only 1 out of every 400 people in the general population is estimated to be a BRCA1/2 mutation holder, with approximately 5-10% of breast cancers at all ages being associated with an inherited gene mutation [1]. Currently the BRCA1/2, ATM, CHEK2, PALB2, TP53, PTEN, CH1, STK11, NBN, NF1 mutations confer increased risk for breast cancer development, warranting the consideration of BPM for risk reduction [2]. Overall, we expect a 12% lifetime risk of breast cancer development in the general population without any risk factors [3]. This risk increases to 45-65% by age 70 in the population of known mutation carriers of BRCA1/2 [1]. BPM has been shown to reduce the risk by roughly 90% in high risk populations [2]; however not all GMCs choose BPM, some may prefer to elect chemoprophylaxis or high-risk surveillance instead. This decision is often determined by patient factors, with a recent study showing that GMCs choosing BPM over surveillance tend to have a college education, income >\$50,000, a first-degree relative with breast cancer, higher total number of relatives with breast cancer, and a prior pregnancy [4].

One reason for this rise may be the downstream effect of popular culture with increasing acceptance for a GMC's surgical choices; Angelina Jolie, through a series of op-ed pieces written for the New York Times and other media outlets, recounted her personal journey with having the BRCA mutation, the passing of her mother from ovarian cancer, and her surgical choices for BPM and reconstruction. She single-handedly has perhaps most profoundly affected

public opinion regarding BPM and amplified awareness for a GMC's breast cancer risk. High profile cases like this have also normalized the idea of having a bilateral mastectomy with reconstruction for risk reduction, while also demonstrating the fact that a woman can still be considered desirable and attractive after this surgery. Today, the modern GMC female interested in BPM expects she will retain her femininity and ability to identify as a beautiful woman post-operatively.

Further complicating this picture, more mutations are being discovered in association with breast cancer, the clinical significance of which are not completely clear. Clinical genetic testing also frequently results in genetic variants of unknown significance (VUS) in genes known to have common mutations with increased risk for breast cancer. As their true clinical significance is uncovered, clinicians must learn how to appropriately integrate this information to guide patient care in this unique and growing population of GMCs.

### **Age: A younger patient has different concerns:**

Frequently woman do not receive a GMC status until after they are diagnosed with a cancer, generally at a younger age. Additionally, many are also being found prior to a cancer diagnosis because of a previously diagnosed family member that underwent that genetic work-up. With these avenues to diagnosis as a GMC, these patients are younger than the average breast cancer patient when they first see a surgeon. This younger age often plays a major role in the decisions these patients make regarding risk reduction surgery and reconstruction. GMCs that elect for BPM and reconstruction tend to have higher aesthetic expectations than those who require the procedure for treatment of active cancer. There are multiple reasons for this, chief among them being that prophylactic surgery is not considered 'life-saving' and that the patients are at a point in life where cosmesis may play a larger factor. The heightened concern for looking 'natural' and 'unoperated' is an ongoing driver for novel surgical treatments when caring for a patient in this cohort.

### **The Relationship of Prophylactic Surgery and High Expectations**

Reconstructive expectations of breast cancer patients have evolved greatly over the past few decades with quality of life and survivorship becoming a central focus. This is especially true when treating GMCs, putting a greater demand on the surgical collaboration required for successful execution. Today, it is not uncommon for patients to expect their post-surgical breasts to improve their appearance and more closely match their desired size and shape than their pre-surgery breast aesthetic. Ultimately, the GMC patient has choices regarding surgical timing, type and the decision to pursue surgery or not, so expectations are inherently high.

Conveying a confident, but realistic depiction of the likely outcomes is important during the pre-operative consultation. Individual patient factors that can influence the final aesthetic outcome such as BMI, current breast size and appearance must be discussed, as well as the possibility of requiring more surgeries (e.g. fat grafting). Patients with realistic expectations of their cosmetic outcomes have been

shown more likely to be satisfied with their BPM results. Additionally, it appears that patients who discuss BPM with their partners prior are more likely to be satisfied with intimacy post-operatively [5].

### Oncologic and Reconstructive Considerations

The goal of BPM in GMCs is risk reduction, and in order to achieve this goal, removal of as much breast tissue as possible provides the best oncologic benefit. A mastectomy while drastically reduces cancer occurrence does not completely eliminate the possibility of breast cancer development in the future. As tissue removal and oncologic benefit increases, risk benefit must be considered as excessively thin mastectomy flaps incur higher risk for ischemia, complicating reconstructive efforts. Adequate flap vascularity is a critical component to successful breast reconstruction, especially single stage, with thicker flaps conferring less risk of ischemia and flap necrosis [6,7]. This relationship between removing the maximum amount of breast tissue while retaining flap perfusion are the competing priorities that surgical oncologists and plastic surgeons must navigate effectively together. Approaching a combined mastectomy/reconstruction patient most importantly requires effective communication between the two surgeons. Additionally, in our institution we employ fluorescence imaging technology in immediate breast reconstruction cases to help quantify perfusion to the flaps [8]. This practice identifies the flaps at risk for ischemia so that the appropriate reconstructive path for each patient can be followed, guiding the decision-making process surrounding whether a patient is more appropriate for one or two stage reconstruction, or delayed reconstruction.

### Novel Reconstructive Techniques

The nipple is generally considered a distinguishing feature of a natural breast. Considering this fact, nipple sparing mastectomy (NSM) continues to be increasingly popular with GMCs. In 2018, a review of the American Society of Breast Surgeons (ASBrS) NSM database showed the majority of NSMs as being performed for prophylactic reasons [9]. Furthermore, NSM patients tend to be younger, Caucasian, and have smaller BMIs [10]. Another study showed higher body image scale scores in NSM compared to skin sparing mastectomy (SSM), but the difference was not statistically significantly [11]. Other studies have also noted higher psychosocial [12] and sexual wellbeing scores in NSM patients [10].

However, NSMs are not perfect; their documented complication rate is low but not insignificant and include possible complications to the nipple areolar complex (NAC) like necrosis, loss, and epidermolysis, in addition to the possible flap infection and necrosis risk seen in all mastectomies. A recent review of the ASBrS NSM database documented a NAC complication rate of 4.4% [9]. Moreover, there is a statistically significant decrease in the measured sensation of the NAC after NSM when compared to control groups [11]. Unfortunately, this reality of a nipple sparing mastectomy is not always completely understood by patients prior to consultation. Explaining these risks and

realities can be more difficult in a patient population that has less tolerance for imperfection because of how it may affect their quality of life. Transparency and informed consent remain critical components to counseling the GMC patient considering BPM.

New techniques in reconstructive surgery may also influence a patient's decision on their surgeon preference. Novel techniques available include the option for prepectoral implant placement, as well as single stage reconstruction, also known as Direct to Implant (DTI). The availability of these techniques to patients depends on several factors, the first of which being plastic surgeon experience with the procedures, the patient's current and desired final appearance, as well as mastectomy flap thickness and viability/perfusion.

Two-stage breast reconstruction using tissue expanders placed subpectorally has been the traditional method for immediate breast reconstruction since the 1970s. However, subpectoral, also known as Dual Plane (DP), placement has disadvantages including animation deformity and pectoralis major origin disruption causing weakened adduction [12]. Reconstructive surgery performed in two stages has drawbacks as well, that DTI circumvents including the avoidance of multiple episodes of anesthesia, and possible reduced cost, as well as reduced pain [13-16]. An evolution of the traditional two stage tissue expander reconstruction created DP DTI, using acellular dermal matrix (ADM) as an inferior sling to support implant placement under the pectoralis major in a single stage surgery [17,18]. Recent studies have demonstrated possible advantages with this technique, including increased patient satisfaction and possible reduction in cost associated with DTI when compared with two stage reconstruction [13-15]. Despite the benefits, DP DTI reconstructions still retain the same issues created by placing a prosthesis subpectoral.

Prepectoral (PP) implant placement resolved the issue of animation deformity caused by subpectoral placement [7,19]. However without routine use of ADM, the technique was classically complicated by high rates of early capsular contracture [20], flap necrosis, implant loss [21], and concern for worsened aesthetics (e.g. implant visibility, rippling) often requiring additional procedures for revision such as fat grafting. One study compared PP placement with and without the use of ADM, the former leading to significantly lower rates of capsular contracture [22]. From our experience, the crucial components necessary for successful PP DTI include initial intraoperative assessment of flap perfusion with sizer in place, followed by the creation of a tight anterior ADM pocket for implant insertion [23]. Use of anterior ADM coverage for implant support and off-loading pressure on the mastectomy flaps prevents the complications traditionally associated with PP [23], while avoiding the disadvantages of DP placement. Despite this, the PP DTI technique has yet to be widely adopted secondary to the lingering concerns over historical complications.

The largest DTI-only comparative study ( $n=134$ ) between outcomes of DP DTI and PP DTI was performed by our group, and showed an overall low complication incidence, with PP DTI complications being slightly less frequent (PP 2% vs DP

12%,  $p=0.07$ ). No implant losses were documented in this study. Furthermore, regarding the concern over increased need for aesthetic revisional procedures in PP patients, no difference was shown in the likelihood of either DP or PP DTI patients to undergo these additional procedures. Last, this study reinforced the positive aesthetic outcomes of PP DTI with a blinded panel scoring PP DTI reconstructions higher than DP DTI in terms of aesthetic outcome [19]. This study effectively corroborated the non-inferiority of PP DTI to DP DTI reconstructive techniques, as well as demonstrated its advantage in better cosmetic outcomes. Because of this, the ability to perform PP DTI could be potentially attractive to patients concerned with aesthetic outcomes when looking for a reconstructive surgeon.

### **Social Media and Patients Sharing Their Story**

Social media plays an ever-expanding role in our lives. There are many online support groups for mutation carriers that easily and immediately connect patients around the world [24]. Within these online groups, and social media in general, now exists a special category of users referred to as 'influencers'. These are users who cultivate a particularly large community of 'followers' with which they share experiences, ideas, products, and influence the general attitudes of those that follow them. It is not uncommon to see an individual sharing their entire experience as a 'mutation carrier,' 'cancer thriver,' or 'cancer survivor' on some form of social media (e.g. Instagram, Facebook, or a blog) [24]. This influence is not confined to the normal events of everyday life, but also extends to health decisions. Since the experiences of one person can be so easily disseminated, the clinical course and opinions of a single patient can disproportionately reverberate throughout the entire community. This process can act as an endorsement for, or dissuasion against, a certain treatment, surgery, or surgeon depending on the level of satisfaction of a single patient. This is particularly important to a surgeon's referral-based practice as the large social media following of certain patients can have greater consequences, both good and bad, to their business than seen historically.

### **Patient Referrals: Our Institution's Recent Experience**

We reviewed our patient database and identified GMCs in the absence of cancer ( $n= 10$ ) that underwent BPM with immediate reconstruction at our institution to better understand how this unique patient population determines where to receive their care. GMCs without a current diagnosis of cancer were of interest as they are inherently less pressured to make surgical decisions. Given they did not have active cancer, they had the advantage of taking as much time as they needed to research online, look for personal referrals, and read online health grade reviews before making their decision. Theoretically, they also had less tying them to a specific institution given no cancer diagnostic information had to be transferred from one institution to another. Patients' referral patterns were reviewed and, if interested, were asked to complete a telephone survey (70% response rate) regarding their decision to pursue surgery at our institution.

When asked about the most important factor regarding these surgeries, the majority of former patients stated that risk reduction was most important to them, however cosmetic outcomes were found to be almost equally as important. Younger patients appeared more concerned with cosmetic outcomes. In regard to novel surgical techniques attracting patients and influencing their decisions, most stated that the possibility of having single stage reconstruction was very appealing to them and was sought out. Knowing that their plastic surgeon was a specialist in prepectoral DTI reconstruction was important to these women. However, not all were offered this option at initial consultation and it did not dissuade their ultimate decision. Many stated that they first chose to undergo consultation at our institution because of internal referrals from physicians they already trusted. Most notably the patients stated their referrals tended to come from OB/GYNs when looking a surgical oncologist, and from the surgical oncologist when looking for a plastic surgeon. This emphasizes the importance of a strong collaborative relationship between the two surgeons. None of the patients had personal referrals from friends or family. Most also stated that they already were comfortable within our institution's network because of care that they themselves, or a family member, had already received here. Remarkably, only a few patients went for second opinions or multiple consultations, and they ultimately avoided those other surgeons because they were either perceived to be 'overly pushy' with their own opinions on whether the surgery was necessary, or made the surgery seem like a 'nightmare' to quote one patient – scaring her about possible complications and the need for multiple surgeries.

The majority stated that the aspect of utmost importance in confirming their decision was feeling confident and comfortable with their surgeons after meeting them for initial consultations. Many women stated that their interactions with both the surgical oncologist and plastic surgeon were very open and honest, especially in taking the time to answer all the patients' questions. They felt a strong personal connection with their surgeons and the warmth they experienced helped build trust, which comforted them and positively influenced their decision to receive care at our institution. For many, the internet and social media served as a resource affirming their decision to receive care at RUMC. One patient detailed that her surgical oncologist was mentioned favorably in Facebook groups, and plastic surgeon was known to have a great reputation online as well, but noted that this did not primarily drive her decision. Approximately one third of the patients looked at online health reviews and ratings for their surgeons prior to committing care to our institution and stated again that these served to positively reinforce their decision.

### **Conclusion**

Overall, the improved understanding of genetic mutation and risk for breast cancer development has created a special population of breast surgery patients. They have different considerations and priorities than the average breast cancer patient when it comes to surgical planning, risk tolerance, and both oncologic and aesthetic outcomes. Younger age

may play a large role in expectations with higher value placed on cosmesis. In response, techniques such as NSM and single stage prepectoral reconstruction are being more commonly used to meet this population's particular demands for excellent outcomes, both oncologic and cosmetic. And though there is significant concern that online reviews, ratings and support groups can influence a patient's decision on where to receive care, the most important determinants lie in the traditional practice of upholding a good bedside manner, developing excellent surgeon-patient rapport, and patient trust in their referring physician.

## Declaration

**Authors Contributions:** AW was the primary author of this manuscript consisting of literature review, manuscript composition and editing. RS contributed significantly to manuscript composition and editing. AM contributed to manuscript development, as well as manuscript revision and editing. AA was the primary contributor to the conception of topic ideas and development of manuscript subject matter, as well as manuscript composition and editing.

**Availability of Data and Materials:** All data used for the completion of this manuscript can be found and accessed using the references section of this manuscript for guidance.

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