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Risk-Reducing Mastectomy—A Review

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Abstract

Mastectomy rates have significantly increased over the last decades, likely due to the rising trend of risk-reducing mastectomies in the treatment and prevention of breast cancer. Growing evidence suggests that aggressive risk-reducing surgical strategies are only justified in high-risk breast cancer situations. Notably, in this selected cohort of women, prophylactic mastectomies offer evident benefit for local and contralateral disease control, and may also provide a survival benefit. Nevertheless, the extent of the increasing frequency of this operation is not explained by the broadening of the medical indications alone. Here we analyze the current evidence regarding risk-reducing mastectomies, its clinical practice, and possible explanations for the rising phenomenon of aggressive surgical locoregional control strategies.

Keywords

breast cancer; risk-reducing mastectomy; prophylactic mastectomy; high risk; BRCA mutation

Introduction

Risk-reducing mastectomy (RRM), also known as prophylactic mastectomy (PM), is performed to reduce the risk of developing breast cancer or breast cancer recurrence. This operation is a growing issue in the treatment of breast cancer with the significant increase in mastectomy rates over the past last decades. A recent retrospective study of data from 1998 to 2011 of the North American National Cancer Database has analyzed the prevalence of mastectomy in the treatment of women with early breast cancer who would traditionally be good candidates for breast-conserving surgery and observed a 5.4% to 29.7% increase in the procedure rate. It seems that the observed change in surgical management is largely due to an increase in bilateral mastectomy for unilateral, early-stage disease [1].

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The validity of the safety of locoregional control of breast-conserving therapy followed by radiation in the treatment of early breast cancer is endorsed by 30 years of solid data, so the phenomenon is not entirely explained by broadening of medical indications.

Furthermore, the indication for a contralateral RRM to prevent metachronous breast cancer seems to be justified, from a medical point of view, only in high-risk situations. In the sporadic breast cancer population, the risk of developing contralateral disease, taking into consideration the improvement in today's adjuvant systemic treatments, is approximately 4% [2]. Considering this low incidence, it is not surprising that a Cochrane Review of the effects of RRM shows no significant survival benefit from a contralateral PM in the sporadic breast cancer patient population [3].

Whether contralateral mastectomy results in improved survival among high-risk breast cancer women who have already had a first breast cancer is still being evaluated. Findings are mixed, but there are increasing data suggesting a survival benefit in this population [3]. Therefore, only small subgroups of patients at high risk of developing in-breast or contralateral breast cancer recurrence have been identified. These patients will probably benefit from unilateral or bilateral RRM. For the other 90% of patients, a cautious approach to these treatments is recommended [4].

A generalized concern has been raised regarding the trend toward an over-aggressive surgical approach to breast cancer because even if RRM is nowadays a routine operation, it still remains a major intervention, with potentially protracted recovery, risk for serious complications, and long-term sequelae. It is therefore very important for physicians to be aware of this tendency, its drivers, and the evidence-based data.

Risk-reducing mastectomy in high-risk patients

It is well known that women carrying BRCA gene mutations have a significant risk of developing breast cancer, with an approximate lifetime risk of 55% to 85% [5].

In the asymptomatic BRCA gene mutation carrier population, bilateral RRM is the most effective option for breast cancer risk reduction. A recent meta-analysis of prospective trials involving more than 2600 patients on the efficacy of RRM in BRCA1 and BRCA2 mutation carriers demonstrated a significant risk reduction in breast cancer incidence (hazard ratio 0.06, 95% confidence interval 0.01–0.41, $p=0.005$) [6]. Debate over whether this intervention also improves survival is ongoing. So far, most studies have limited follow-up periods, and it is not clear what impact on survival there will be decades after bilateral RRM, even if there are increasing data suggesting a survival benefit in this population [3].

Women with newly diagnosed breast cancer or who are breast cancer survivors comprise a special BRCA mutation carrier category. These patients have a higher risk of local failure after breast-conserving surgery compared to women with sporadic breast cancer. However, it is not clear if this difference correlates with a statistically significant difference in breast cancer-specific survival and overall survival [3, 7]. It is also still uncertain whether RRM improves either breast cancer-specific or overall survival in BRCA gene mutation carriers. Modeling studies predict this will be observed over time [8]. Nevertheless, the local

treatment of breast cancer in these high-risk patients is nowadays usually a mastectomy [9]. Even performing a contralateral RRM up front is a reasonable option in the mutation carrier group, since the expected cumulative lifetime risk of contralateral breast cancer is 20% to 83%, compared to 4% in the general breast cancer patient population [2]. In a prospective Dutch multicenter cohort study, BRCA1/2 mutation carriers with breast cancer had significantly improved overall survival after contralateral PM (8% versus 19%, $p < 0.001$) [10].

Determinants of choice

The 30% prevalence of mastectomy in early-stage breast cancer and the 11% prevalence of bilateral mastectomy for unilateral breast cancer are not well explained by the approximately 10% prevalence of mastectomy in high-risk breast cancer women. We must assume that the majority of breast cancer patients who undergo unilateral and bilateral RRM have an average-risk situation [1]. A survey conducted by the Detroit and Los Angeles SEER database of women undergoing contralateral RRM confirmed that the majority of patients (68.9%) who received a contralateral RRM had no genetic or familial risk factor for contralateral disease.

One of the strongest factors associated with RRM was patient choice. Nearly 80% of the women who chose to remove the non-affected breast stated that their strongest motivation in opting for this operation was fear of recurrence. In a study of the decision-making processes of women having contralateral RRM, the desire to reduce the risk of contralateral breast cancer, obtain “peace of mind”, improve survival/extend life, and desire to prevent metastatic disease were identified as the most important reasons for undergoing the operation. Interestingly, nearly all these women were aware that undergoing a bilateral mastectomy would not lead to a survival benefit. The authors suggest that this discordance is due to anxiety and fear experienced by patients during the decision-making process. Women tend to overestimate the actual chance of developing a breast cancer recurrence or a contralateral cancer [11]. This unrealistic fear of recurrence reflects the findings of other studies [12, 13]. The RRM decision-making process skips the rational, cognitive pathway and seems to be primarily based on emotion [11, 13, 14].

Physicians are an important source of information for patients. Therefore, while counseling patients on risk-reducing surgery, physicians should be aware of the strong role of patient emotions in this setting, and should take both risk statistics and these patient emotions into account in order to avoid overtreatment.

Surgical and reconstructive techniques

Surgeons performing RRM have several surgical options. The radical mastectomy (RM) is rarely performed today as a risk-reducing procedure following the advent of nipple-sparing mastectomy (NSM) and skin-sparing mastectomy (SSM). In both of these techniques, the breast tissue is removed, preserving the breast skin envelope. In SSM, the nipple-areola complex (NAC) is removed en bloc with the breast, whereas it is spared in NSM.

In comparison to SSM, the nipple-sparing procedure allows superior cosmetic outcomes, better body image, and better sexual functioning [15]. In both procedures, breast reconstruction is planned for immediately in order to prevent the shrinking of the skin envelope. The reconstruction can be performed with implants or autologous tissue depending on the patient's characteristics and preferences. Completion of breast reconstruction may take a long time, up to 1–2 years, and may include additional aesthetic corrections, such as lipofilling and nipple reconstruction.

However, due to the maintained NAC and the underlying small amount of breast tissue needed for its vascularization, there are concerns about the residual breast cancer risk. There is evidence that the preservation of the NAC is not an obstacle to achieving an acceptably low breast cancer risk, and that it is even is oncologically safe, with no increased risk of local recurrence, in women with sporadic breast cancer [16]. Whether this is also true for BRCA mutation carriers is still open to debate [17, 18].

RRM with reconstruction is a major surgical procedure; available data suggest that 30% to 40% of women treated with this kind of operation will experience complications, and that some of will require re-operation [19, 20].

After RRM, women do report reduced cancer distress and anxiety, but the effect of the procedure on a woman's body image, and worse-than-expected cosmetic outcomes, are a relevant concern [11].

A study of asymptomatic BRCA mutation carriers after RRM found that even 2 years after surgery, 37% of women reported that their breasts felt unpleasant, 29% were not satisfied with their breast appearance, and 21 % felt embarrassed about their naked bodies [21]. Therefore, quality-of-life issues should be openly addressed during counseling in order for women to form realistic expectations [21].

Nevertheless, overall patient satisfaction with the decision to undergo RRM is as high as 80%, and the vast majority would choose RRM again [11].

Conclusions

RRM is the most effective risk-reducing intervention to prevent breast cancer and breast cancer recurrence. Nevertheless, its effect on survival has yet to be determined.

The risk of developing the disease differs greatly among women and is primarily based on a woman's risk situation. An increasing amount of evidence suggests a survival benefit for bilateral RRM in BRCA mutation carriers, but no significant survival benefit for contralateral RRM in non-carriers.

However, the global trend toward increasing use of RRM is a clear signal that when it comes to risk-reducing procedures, patient choices are mainly emotion-driven and not rational. The challenging task for now and the future is the appropriate counseling of women regarding these issues.

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