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Prophylactic Mastectomy: A boon or bane?

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Abstract:

Globally, breast cancer is the second most common cancer next only to lung cancer and a major public health challenge to women's health. Worldwide, breast cancer affects 1.3 million women every year which represents 23% of all cancers in women. It is estimated that by 2030 the global burden of breast cancer will increase to over 2 million new cases per year. Unlike other cancers, breast cancer is treatable if detected at an early stage. Management of women who carry a high lifetime risk for breast cancer is always an issue of debate. A number of risk-reducing treatment options with varying efficacy exist, including regular surveillance, chemoprevention, and prophylactic surgery. Prophylactic mastectomy (PM) or Risk reducing mastectomy (RRM) remains a controversial procedure as a preventive tool against breast cancer. More women are opting for prophylactic mastectomy as

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a risk reducing strategy for breast cancer. Prophylactic mastectomy is appropriate only for a small proportion of women who are at high risk for breast cancer. Patient misconceptions about recurrence risk and fear have been implicated in the increase in prophylactic procedures. Other possible reasons for the rise in prophylactic mastectomy are highly sensitive breast cancer screening methods, which diagnose breast cancer at earlier stages, and improved breast reconstruction techniques. With this background this paper aims to analyze the pros and cons of preventive mastectomy.

Key words: Prophylactic mastectomy, Risk reducing strategy, breast cancer.

Introduction:

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females worldwide. An estimated 1.38 million women across the world were diagnosed with breast cancer in 2008, accounting for nearly a quarter (23%) of all cancers diagnosed in women and represented 11% of total cancer in men and women.[1] The rapid development of genetic counseling clinics and better diagnostic techniques for hereditary cancers has dramatically led to the rise in statistics of women at risk and requiring prophylaxis. A number of risk-reducing treatment options with varying efficacy exist, including regular surveillance, chemoprevention, and prophylactic surgery.[2] Prophylactic surgeries include prophylactic mastectomy and prophylactic salphingo-oopherectomy. More women are opting to have their breasts removed to reduce the risk of cancer. Unfortunately many women who overestimate the risk of developing breast cancer undergo unnecessary surgery. There by, prophylactic mastectomy remains a controversial risk reduction measure for breast cancer.

What is prophylactic mastectomy?

Prophylactic mastectomy or Preventive mastectomy (PM) (or risk-reducing mastectomy) is the surgical removal of one or both breasts to prevent or reduce the risk of breast cancer in women who are at high risk of developing the disease.[3] It is of three types: total mastectomy, subcutaneous mastectomy and skin sparing mastectomy. Total mastectomy involves the removal of entire breast along with nipple. In Subcutaneous mastectomy, breast tissues are removed leaving the nipple intact. In skin sparing mastectomy, most of the skin over the breast (other than the nipple and areola) is left intact. Preventive mastectomy may be bilateral or contra lateral. It can be done along with oopherectomy, and with or without the reconstruction of breast.

Criteria for prophylactic mastectomy:

Eligibility criteria for prophylactic mastectomy are based on one of the following categories:

- A known mutation of BRCA 1 or BRCA2 or other strongly predisposing breast cancer susceptibility genes like CHEK2 mutation
- A family history of breast cancer in multiple first-degree relatives and/or multiple successive generations of family members with breast and/or ovarian cancer (family cancer syndrome)
- Personal history of breast cancer
- High-risk histology: Atypical ductal or lobular hyperplasia, or lobular carcinoma in situ confirmed on biopsy.[4]

Uptake of prophylactic surgery:

There was a wide variation in uptake of prophylactic surgery worldwide. In a recent survey, the largest uptake of prophylactic mastectomy with breast reconstruction was found in the United States of America (36.3%).[5] Average age at the time of prophylactic mastectomy/breast reconstruction among high-risk women was found to be 35-46 years (range 20-73).[6-10] And they were significantly younger and with higher educational level.[11,12] Mutation carriers among PM acceptors ranges from 13 to 100 % and other breast cancer risk carriers were in between 55-100%, and the majority of women who underwent PM did not have personal history of breast cancer (92-100%).[7, 9,13,14] Majority (63-100%) of the high-risk women had opted for breast reconstruction after prophylactic mastectomy[7,8,14,15] and 14-63% of women who underwent prophylactic mastectomy also opted for prophylactic salphingo oopherectomy.[9,16,17]

Increasing prophylactic mastectomy rates:

Prophylactic mastectomy with reconstruction is becoming an increasingly popular choice among women accepting for PM. Most women who are diagnosed with cancer in one breast have a very low risk of developing cancer in their other breast. Patient fear is one of the main motivational factors for prophylactic surgery without truly examining the actual chances of developing cancer.

Accepting prophylactic mastectomy was highly a personal decision. Factors that determine the high risk women to consider for prophylactic surgeries are fear, over estimation of perceived risk, personal characteristics features including her experience with cancer within her family; her role and responsibilities in her nuclear family; her values; her experiences with the medical system; and her

misconception about cancer risk. Other possible reasons for the rise in prophylactic mastectomy are more sensitive breast cancer screening methods, which diagnose breast cancer at earlier stages, increased awareness, insurance coverage, underestimation of the extent of this major surgery and improved breast reconstruction techniques. High-visibility celebrities with breast cancer who have chosen to have prophylactic mastectomies are also playing an important factor for choosing the surgery.

Worry about breast cancer and perceived risk were independent predictors of prophylactic mastectomy.[18-20] Parenthood also plays an important role in the selection of PM. Meijers-Heijboer HJ et al reported that 61% of women with children selected risk reducing mastectomy compared with 14% women without children (odds ratio-9.43; Confidence Interval-1.92 TO 46.4;P=.006).[21] Yi M et al reported that majority of patients (72%) chose to undergo contralateral PM for the following reasons: a family history of breast cancer, difficulty in surveillance, and fear of developing another breast cancer.[22] An increasing trend for prophylactic mastectomy was observed. The rate of increase in prophylactic mastectomy ranges from 20% to 188%.[11,12,23-25] Adherence to published consensus guidelines for the indications of prophylactic mastectomy was observed to be 97.6%.[26]

Among unaffected women waiting for genetic report, the rate of consideration for prophylactic mastectomy, if BRCA found to be positive varies from 19 to 23%.[27,28] At the same time among unaffected high risk women, consideration range from 3 to 55%.[21,29] These broad differences might be due to difference in sample size, assessment strategies ,different follow up preferences, cultural differences, differences in health-services delivery systems, differences in medical specialties which facilitated the

discussions of follow-up options, or differences in the type of follow-up information provided. Many women overestimate their risk. Studies have reported that women overestimate their breast cancer risk both in genetics clinics and in general practice.[30]

Perceptions after surgery

Women who undergo prophylactic bilateral mastectomy have an exaggerated perception of their breast cancer risk before surgery. About 70-100% of women who underwent prophylactic mastectomy were satisfied with the surgery[7,8,10,14,31,32] and 5% reported regrets for choosing the surgery as an option.[31] Generally, 48-55% of all women felt less sexually attractive after prophylactic mastectomy[7,33] and 32-69% of them experienced untoward changes in their sexual relationship[9,32,33] Changes in the sexual relationship seemed independent of type of PM or presence or absence of breast reconstruction.[32] Around 12-53% of the women reported adverse effects on the appearance of their body i.e. were self-conscious about their appearance, felt less physically attractive, were dissatisfied with their body, as a result of prophylactic mastectomy [6,7,10,32,33] and an equal proportion of women reported a change in feelings of feminity.[6,7] Dissatisfaction with the surgical scars was reported by a third to almost half of all women (33-44%) who underwent the surgery.[7,33] Moreover, women without breast reconstruction were less satisfied with their bodies than women with breast reconstruction.[7,32] But Brandberg Y et al. reported that majority of the women were satisfied with their surgery, but a considerable proportion reported feelings of depression and some impact on their sexuality.[33]

Complications of prophylactic mastectomy

It includes pain, bleeding, infection, development of scar tissue, cutaneous necrosis, capsular contractures, hematoma, implant rupture and implant malposition. Cutaneous necrosis and capsular contractures were observed in approximately 30% of cases, especially when the glandular tissue has been removed close to the dermis.[34] Jose Abel de la Pen˜a-Salcedo et al reported that capsular contracture was found in 6.25% of women who underwent PM, hematoma was observed in 3.12% women, and 1.56% had infection.[35] Overall one third of all women were having complications of prophylactic mastectomy.[36]

Efficacy of prophylactic mastectomy:

Average gain in life expectancy ranges from 2.8 to 11.7 years depends upon her cancer risks and her age.[37,38] Gain in life expectancy declined with the age of the woman at the time of surgery. Gain was minimal for women aged 60 years and older. It was demonstrated that risk reducing mastectomy was cost effective compared to other medical interventions. The incremental cost per life year saved, ranges from $800 to $73,755 depends upon age and other risk status.[39]

Table 1: Efficacy of Prophylactic mastectomy (PM)

Article	Group	Subgroup		Follow up
Kaas et al.[40]	254 BRCA mutation carriers –All Underwent PM	With diagnosis of breast cancer before surgery	107	1(0.93% Incidence of cancer)
		Unaffected group	147	0(100% risk reduction)
Meijers-Heijboer H et al.[21]	139 Women with BRCA carriers	Opted for PM	76	0(100% risk reduction)
		No PM	63	8(12.7% Incidence of cancer)
Domchek SM, et al.[41]	2482 Women with BRCA carriers	Opted for PM	247	0(100% risk reduction)

		No PM	2235	7% Incidence of cancer
Heemskerk-Gerritsen et al.[42]	570 *BRCA* mutation carriers	Underwent PM	212	1(0.47% Incidence of cancer)
		No PM	358	61(17.04% Incidence of cancer)
Skytte et al.[43]	307 *BRCA* mutation carriers	Underwent PM	96	0.8%Incidence of cancer
		No PM	211	1.7%Incidence of cancer
Arver et al.[44]	223 *BRCA* mutation carriers	Underwent PM		0(100% risk reduction)

Most studies concur that prophylactic mastectomy provides upto 100% reduction.

Ethical issues in prophylactic mastectomy:

The procedures do not completely eradicate cancer risk because, often, not all the tissues at risk are removed. It is also important to keep in mind that prophylactic mastectomy doesn't guarantee a cancer-free future. There are four main ethical issues. First of all, it's a risky condition, not a disease for which surgery is a prophylactic option. Having one or both breasts removed is a major surgery. Some encourage the surgery as a protective measure, while others believe that there is no sufficient evidence to support its benefits. Secondly, the cause of the risk is a genetic factor and some might argue about genetic 'exceptionalism'. Thirdly, there is no organ as, connected to feminity, sensuality, sexuality, adulthood and motherhood as the breast. Lastly, making tough and complex choices requires assistance from ethics. Areas of agreement: Among ethical principles, western countries often rely on autonomy. Area of controversy: In France during 1998, national recommendations set a list of criteria to fulfill, reducing autonomy.[45]

Alternative risk reduction strategies:

These include regular surveillance and chemoprevention. Regular surveillance includes monthly breast self-examinations, clinical breast examination, periodic mammograms (conventional or digital), automated whole breast ultrasound, molecular breast imaging and Magnetic Resonance Imaging (MRI). Newer imaging techniques such as digital tomosynthesis, positron emission mammography, Vibro-acoustography, breast computerized tomography and 3D whole breast ultrasound are under evaluation. Chemo-preventions using Tamoxifen or Raloxifene like medication are used to reduce the breast cancer risk.

Table 2: Summary of alternate risk reduction strategies

Risk reduction measures	Criteria	Studies	Benefits	Limitations/Draw backs
Self breast examination (SBE)	Monthly breast self exam is an option for women starting in their 20s.[57]	Kösters J.P et al.[46]	Easiest method	Least precise. Increased number of unnecessary biopsies. SBE has not been found to decrease risk of dying from breast cancer.
Clinical breast examination (CBE)	Women in their 20s and 30s should have a CBE preferably every 3 years. Starting at age 40, it should be done every year.[57]	Bobo JK et al[47], Alexander FE, et al[48] and Shapiro S[49].	3% to 45% detection rate of cancer	CBE is complementary to screening mammography, it does not replace it. CBE have not been found to decrease risk of dying from breast cancer.
Mammography	Women age 40 and older should have a mammogram every year.[57]	Fracheboud J et al[50], Alexander FE et al[48] Breen N et al[51] and Kuhl CK et al.[52]	26 % to 60% detection rate	It cannot prevent cancer, radiation risk, occasionally misses a cancer, over-diagnosis & treatment. It is not indicated for younger women.
High frequency breast USG	Women with dense breast.[57]	Kuhl CK et al[52].	39.5% detection	Requires a well-trained and

			rate among women with dense breasts [17], distinguish fluid-filled cyst from a solid mass, no radiation risks	experienced sonologists, difficult distinguishing between abnormality and surrounding tissue, Cannot show micro-calcifications
MRI	Women at high risk (greater than 20% lifetime risk) should get an MRI every year.[57]	Kuhl CK et al[52].	90.7% detection rate among all women	Expensive, not widely available, low specificity.[58]
Chemoprevention-Tamoxifen	Women at high risk for breast cancer.[57]	Fisher B et al[53], Veronesi U et al[54] and King MC et al[55].	No reduction in breast cancer to 62% reduction among BRCA 2 carriers	Venous thrombo embolism, endometrial cancer and cataracts, bone loss in premenopausal women
Raloxifene	Postmenopausal women at high risk for invasive breast cancer.[57]	Cummings SR et al[56].	65% reduction in breast cancer	Flushes, leg cramps, thrombo-embolic events.

Each risk reduction measure is having its own merits and demerits. Relying on single method is also not currently indicated in any literature

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Genetic counseling:

Before prophylactic mastectomy, efforts must be made to correct any overestimation of risk and also to allay excessive anxiety through genetic counseling. This counseling should include the ascertainment of medical and family histories, determination and communication of cancer risk, assessment of risk perception, education regarding the genetics of breast cancer and the necessary follow-up. Psychological assessment may also be warranted. The genetic counselor

should provide an individualized estimate of a woman's risk of breast cancer and discuss other preventive options. And the woman should be encouraged to take her time to consider a decision. Reports from Van Dijk et al[19] states that before the counseling, 83% of the low-risk women overestimated their risk and after counseling 56% overestimated their risk. Perceived risk was found to be decreased after the counseling session.

Conclusion:

Prophylactic mastectomy is becoming an increasingly frequent procedure. There is plenty of evidence that prophylactic mastectomy lowers the risk of breast cancer in at least 95% of the high-risk population. Although prophylactic mastectomy may be appropriate in women at high risk of developing breast cancer, it is perhaps less so in those who have a moderately increased risk. Such moderate-risk women are likely to get benefit from interventions aimed at reducing breast cancer anxiety and correction of exaggerated breast cancer risk perceptions. Cancer risk assessment is an important decision-making tool for women considering irreversible risk-reducing surgery. So, proper risk assessment and genetic counseling is necessary to make a correct decision for those at increased risk of breast cancer.

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