Nipple-Areolar Complex Sparing Mastectomy - A Realistic Hope to Improve Prophylactic Mastectomy Acceptance in BRCA Mutation Carriers?

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Incidence of Breast cancer has increased over the last decade due to increased public awareness of breast cancer screening. Although more patients present early nowadays with smaller tumors due to early detection, up to 70% of breast cancer patients in Hong Kong received mastectomy [1]. This is due to the relatively small breast size in Asian population. Nipple-areolar complex sparing mastectomy (NSM) was first described and performed by Rice and Stickler for benign disease with preservation of skin and the nipple-areolar complex (NAC) [2]. With an increasing demand for better quality of life in breast cancer patients after mastectomy, interest in NSM has been reignited in the recent decade [3]. As an alternative to conventional total mastectomy, it offers cosmetic advantages to selected patients. However, concerns over the risks of Locoregional Recurrence (LR) in the skin flap or NAC and surgical complications associated with NSM have limited its extensive application.

Before discussing the feasibility of NSM in BRCA mutation carriers, it is prudent to review its oncologic outcomes in sporadic patients. Two large systematic reviews have attempted to evaluate the clinical outcomes of NSM in breast cancer treatment. In the review published in 2013 [4,5], with medium follow-up duration of 49.3 months (Range 0.2-156 months), Mallon et al. reported a pooled skin LR rate of 4.2% (0%-19.2%) and pooled NAC LR rate of 0.9% (0%-12%) [4]. In the more recent systematic review involving 36 more studies, Headon et al. found a lower pooled LR rate of 2.38% in patients receiving NSM, which was concluded to be comparable to that in conventional mastectomy [5]. Similar results have been observed in a recent single-centre study in Taiwan which yielded similar local recurrence and surgical complication rates to the western data [6].

In general, proper patient selection is the key to reduce local recurrence; commonly used selection criteria include single tumour of less than 2cm size, tumors-to-areola distance of more than 2cm, estrogen and progesterone receptor positive, human epidermal growth factor-2 (HER-2) negative and no lymph vascular invasion.

Apart from ontological safety, surgical complications including nipple necrosis remains an important concern of NSM. Headon et al. reported an overall complication rate of 22.3% with a nipple necrosis rate of 5.9% [4]. Orzalesi et al. reported an overall NAC necrosis rate of 4.8% [7]. Suggested risk factors include smoking, neoadjuvant breast irradiation, positive retroareolar margin and obesity [7,9]. Vascular pattern on pre-operative MRI may predict likelihood of nipple necrosis [10]. Other complications include reconstruction failures, wound dehiscence and surgical site infection [7].

NSM is generally considered safe in sporadic breast cancers, but in individuals with high hereditary risks of breast cancer like in BRCA1 or BRCA2 mutation carriers, the estimated cumulative lifetime risk for invasive breast cancer were estimated to be as high as 85% in 1990s [11]. In more recent retrospective studies, the lifetime (up to 70 years) breast cancer risks for BRCA1 or BRCA2 mutation carriers are estimated to be around 55% to 65% for BRCA1 and around 45% for BRCA2 [12,13]. Prophylactic mastectomy has been shown to offer reduction of breast cancer risk by 90-95% in BRCA1/2 mutation carriers [14]. While such risk has been reported to be higher among Asian comparing to white female mutation carriers [15], local data showed that only 17.7% of a Hong Kong Chinese cohort opted for prophylactic mastectomy [16]. Recent advancements in nipple-sparing mastectomy may provide an alternative surgical option for risk reduction with better cosmetic outcomes. Reynolds et al. studied 33 BRCA mutation carriers (62 breasts) who underwent mastectomy and found no evidence of atypical ductal hyperplasia, in-situ or invasive cancer in all 33 prophylactic mastectomy specimen. Of the 29 specimens rejected for cancer treatment, only 2 (7%) had malignancy and 1 (3%) had atypical at the NAC [17]. A recent study in 2015 reviewed 201 BRCA mutation carriers (397 breasts) who received NSM for cancer treatment or prophylaxis with a mean follow-up...
duration of 32.6 months (Range 1-76 months). A total of 4 cancer events including 3 in the cancer group and 1 in risk reduction group occurred after the NSM, with none occurring in the NAC [18].

Based on the best available evidence, NSM is oncologically safe with superior cosmetic outcome in carefully selected patients. In localities with low prophylactic mastectomy acceptance rate among the BRCA 1/2 mutation carriers such as in Hong Kong and other parts of Asia, this technique is likely to make a remarkable impact and gain better acceptance in foreseeable future.

References