Occult Pathology Detection in Contralateral Prophylactic Mastectomy: Risk Predictors and Outcomes in 118 Consecutive Bilateral Mastectomies

Occult Lesions in Prophylactic Mastectomy

Adnan Gundogdu[1], Merve Aktas[2], Kubra Ertekin[3], Merve Tokocin[4], Osman Cem Yilmaz[5]

[1]Department of General Surgery, Sancaktepe Şehit Prof.Dr. İlhan Varank Training and Research Hospital, Istanbul, Turkey
[2]Department of General Surgery, Bayburt State Hospital, Bayburt, Turkey
[3]Department of General Surgery, Afyonkarahisar Health Sciences University Faculty of Medicine, Afyonkarahisar, Turkey
[4]Department of General Surgery, Bağcılar Training and Research Hospital, Istanbul, Turkey
[5]Breast Surgery, Istanbul Breast Center, Istanbul, Turkey

Introduction: Contralateral prophylactic mastectomy (CPM) is increasingly chosen by young and high-risk breast cancer patients, leading to more extensive surgery whose true benefit remains difficult to clarify. Occult malignant or high-risk lesions may be detected in CPM specimens, but reported rates and risk predictors are inconsistent. We aimed to determine the frequency of occult pathology and identify clinicopathologic and imaging factors associated with high-risk disease in a consecutive cohort of bilateral mastectomies.

Methods: Retrospective analysis of 118 consecutive bilateral mastectomies including invasive carcinoma with CPM (n=92), bilateral prophylactic for genetic/familial risk (n=17), and high-risk lesions (n=9). BRCA1/2 mutations affected 32.3% (BRCA1 19.8%, BRCA2 12.9%). Data encompassed demographics, genetic testing, imaging (BI-RADS, MRI, mammography, ultrasound), histopathology, and neoadjuvant outcomes. Statistical associations were evaluated using multivariable logistic regression ($p < 0.05$). All underwent preoperative MRI, mammography, and breast ultrasound with immediate implant-based reconstruction .

Results: Mean age was 44.2 ± 8.4 years (n = 118), and 78% of patients were premenopausal. In 92 patients with invasive carcinoma undergoing CPM, contralateral occult pathology was detected in 19.6% (18/92): DCIS 6.5%, ADH 6.5%, ALH 3.3%, and fibroadenoma 3.3%. Primary tumor analysis revealed a DCIS component in 47.5% (56/118), which was strongly associated with BRCA mutations (OR 3.2, 95% CI 1.6–6.4; $p < 0.001$) and family history (OR 2.1; $p = 0.022$), and correlated with higher invasive grade (2.3 ± 0.8 vs 1.9 ± 0.7; $p = 0.005$; $r = 0.41$). Multivariable logistic regression identified BRCA mutations (OR 3.1), BI-RADS > 4 (OR 2.5), and age < 50 years (OR 1.8) as independent predictors of occult/high-risk pathology (model $R^2 = 0.35$). BRCA mutation carriers demonstrated higher pCR rates after neoadjuvant chemotherapy (38.5% vs 20.7%; OR 2.4; $p = 0.009$). Nipple-sparing mastectomy was achieved in 87–91% of procedures across subgroups. Patient anxiety and personal preference accounted for 41.3% of CPM decisions in unilateral invasive cancer patients. Among purely prophylactic bilateral mastectomies (n = 17), 8 patients (47.1%) were BRCA1/2 mutation carriers, 4 (23.5%) had other high-risk germline variants, 2 (11.8%) were gene-negative with a strong family history, and 3 (17.6%) underwent surgery based solely on patient anxiety and personal preference. In an additional subgroup of 9 women with previous high-risk lesions (DCIS, LCIS, or ADH), one gene-negative patient with LCIS in one breast and imaging-suspicious but biopsy-negative DCIS in the contralateral breast was found to have occult invasive carcinoma in the breast with prior DCIS suspicion at final pathology.

Characteristics of Patients with Unilateral Invasive Cancer Undergoing CPM (n = 92)

Variable	Total (n=92)	Occult pathology present (n=18)	Occult pathology absent (n=74)	p-value
Age, years (mean ± SD)	43.8 ± 8.1	40.2 ± 6.9	44.7 ± 8.3	0.018
Age < 50 years	72 (78.3%)	18 (100%)	54 (73.0%)	0.011
Premenopausal	72 (78.3%)	17 (94.4%)	55 (74.3%)	0.067
BRCA1/2 mutation	34 (37.0%)	13 (72.2%)	21 (28.4%)	<0.001
Strong family history	48 (52.2%)	14 (77.8%)	34 (45.9%)	0.019
Patient anxiety / patient-driven decision	38 (41.3%)	12 (66.7%)	26 (35.1%)	0.021
Contralateral BI-RADS ≥4	31 (33.7%)	11 (61.1%)	20 (27.0%)	0.007
Primary tumor grade (mean ± SD)	2.2 ± 0.8	2.6 ± 0.7	2.1 ± 0.8	0.008
DCIS component in primary tumor	44 (47.8%)	15 (83.3%)	29 (39.2%)	0.001
Neoadjuvant chemotherapy	48 (52.2%)	11 (61.1%)	37 (50.0%)	0.413

Abbreviations: CPM, contralateral prophylactic mastectomy; DCIS, ductal carcinoma in situ; ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; BI-RADS, Breast Imaging Reporting and Data System;; SD, standard deviation.

**Categorical variables are presented as number (percentage). Continuous variables are presented as mean ± standard deviation.*

Discussion: Detection of occult pathology in nearly one-fifth of CPM cases supports its potential value in carefully selected patients. The presence of a DCIS component in the index tumor was closely linked to more aggressive biology and underlying hereditary risk, suggesting a subgroup that may benefit from intensified surveillance and risk-reducing strategies. In the high-risk lesion subgroup, a gene-negative patient with LCIS in one breast and imaging-suspicious but biopsy-negative DCIS in the contralateral breast was ultimately found to harbor occult invasive carcinoma, highlighting the importance of careful management of radiologic–pathologic discordance. Genetic predisposition, strong family history, and patient anxiety were major drivers of prophylactic decisions in this predominantly young, premenopausal cohort. The favorable neoadjuvant response observed in BRCA carriers and the performance of our multivariable model together provide preliminary support for a more personalized approach to contralateral risk assessment in hereditary breast cancer.

Conclusion: Occult pathology was found in almost one-fifth of CPM specimens, supporting its potential value in carefully selected patients. A DCIS component in the index tumor was closely linked to more aggressive and hereditary tumor biology, while genetic risk, strong family history, and patient anxiety were major drivers of prophylactic decisions in this young, premenopausal cohort. The favorable neoadjuvant response in BRCA carriers and our risk model together suggest that contralateral prophylactic surgery should be guided by individualized risk assessment rather than a one-size-fits-all approach.

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