Sentinel lymph node biopsy should be considered for clinically node-negative breast cancer regardless of *BRCA1/2* mutation status

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Background: *BRCA1/2* mutations lead to an elevated risk of breast cancer. None involved in whether *BRCA1/2* mutation status will affect the first decision-making of sentinel lymph node (SLN) biopsy or not for clinically node-negative breast cancer. We retrospectively investigated whether *BRCA1/2* mutation status influenced SLN involvement rate and survival outcomes after sentinel lymph node biopsy (SLNB) for Chinese clinically node-negative breast cancer patients.

Methods: Patients who underwent SLNB at initial were enrolled and divided according to *BRCA1/2* mutation status. Germline DNA for *BRCA1/2* testing was derived from blood samples. SLN involvement rate and clinicopathological characteristics were analyzed using the Chi-square test. Kaplan–Meier univariate and multivariate Cox regression analysis was performed to compare survival between groups.

Results: According to *BRCA1/2* mutation test criteria, 156 Chinese women receiving initial SLNB with clinically node-negative breast cancer were selected—thirty-one patients identified as *BRCA1/2* mutation carriers and 102 as non-carriers were enrolled. Non-carriers seemed to be with a more advanced TNM stage ($P<0.01$) compared to the non-carrier group. Once SLN involved, the patient will receive axillary lymph node dissection in which *BRCA1/2* mutation did not increase the rate ($P=0.73$). Disease-free survival (DFS) ($P=0.48$) and recurrence-free survival (RFS) ($P=0.79$) are comparable between groups, even after adjustment for clinicopathological characteristics, systemic treatment, and surgical management of breast [DFS, hazard ratio (HR) =1.63, confidence interval (CI): 0.48–5.54, $P=0.43$; RFS, HR =0.75, CI: 0.14–3.89, $P=0.73$].

Conclusions: SLNB should be considered for clinically node-negative breast cancer regardless of *BRCA1/2* status.

Keywords: Sentinel lymph node biopsy (SLNB); clinically node-negative breast cancer; *BRCA1/2* mutation; sentinel lymph node involvement rate (SLN involvement rate); survival

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Introduction

Breast cancer is, by far, the most common malignancy in women worldwide (1). The stage at diagnosis and biological features help in determining prognosis. Surgery is always the primary treatment approach, and axillary lymph node staging is essential for evaluating the prognosis and planning the treatment. Completion axillary lymph node dissection (cALND) may lead to complications, including upper limb lymphedema, sensory numbness, and shoulder joint activity disorder, which could affect the patient's quality of life (2). For this reason, sentinel lymph node biopsy (SLNB) has widely replaced cALND as routine axillary staging for patients with breast cancer with a clinically negative axilla according to the recommendations of the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32 Randomized Phase 3 Trial (3). Still, both Kim *et al.* (4) and Veronesi *et al.* (5) identified the safety of SLNB and recommended it should be the treatment of choice for patients who have early-stage breast cancer with clinically negative nodes.

Germline mutations in breast cancer susceptibility genes have become factors that influence the care of breast cancer patients. Surgeons are, therefore, required to integrate this information into surgical management decision-making (6). *BRCA*-associated breast cancer is the most common type of hereditary breast cancer, which can differ from sporadic breast cancer in both screening (7) and prevention. As Robson (8) reported increased both ipsilateral and contralateral risk of breast cancer for *BRCA1/2* carriers, even breast-conserving therapy remains a relative contraindication to patients with breast cancer with *BRCA1/2* predisposition according to the National Comprehensive Cancer Network guidelines version 2.2020 (9). Published study has reported worse outcome for patients with a *BRCA1* or *BRCA2* mutation compared with patients with sporadic breast cancer (10). Due to that the increased risk of breast cancer might result in easier metastasis of lymph node, it is still unknown that whether the possible worse prognosis with *BRCA1/2* mutation would have effect on SLNB.

Several studies (11,12) have addressed the association between different *BRCA1/2* mutation status and different strategies for surgical management of the breast (13,14). Practice guidelines have also addressed the prognostic impact of germline *BRCA1/2* mutations on different surgical managements for the breast (i.e., breast-conserving therapy versus mastectomy) and have provided strategic suggestions (6,15). However, none involved the association between *BRCA1/2* mutation status and the surgical management of the axilla.

Since cALND was the only option before SLNB was introduced in the early 1990s (16). Globally, SLN biopsies have been widely accepted only within the last ten years, but shorter in China only in the past five years. That is why none reported whether it is suitable that early breast cancer patients with *BRCA1/2* mutation received SLNB. A study that enrolled patients between 1970 and 2003 did not include patients treated with SLN biopsies because these procedures were not practiced during this period (17). Even the American College of Surgeons Oncology Group Z0011 randomized trial (18) and Mansel *et al.* (19) did not stratify patients on the *BRCA1/2* mutation status, likely following information on carrier status not being available from May 1999 to December 2004 (20). There is no such study in the Chinese population either.

According to the guidelines of the American Society of Clinical Oncology (ASCO), breast cancer patients with clinically negative axillary nodes are candidates for SLNB for axillary staging (21). However, the indications for SLNB are clinically node-negative breast cancer, additional factors that may also affect the decision to perform SLNB, which may influence the SLN involvement rate, and the prognosis (22). *BRCA1/2* mutation status has not been one factor affecting SLNB for clinically node-negative breast cancer patients.

Genetic testing is not as frequent in China as it is in western countries. Chinese breast cancer patients with unknown *BRCA* mutation status receive SLNB if eligible because of the first presentation with clinically negative nodes. Among these, both *BRCA1/2* carriers and non-carriers receive SLN biopsies. However, it is unknown whether *BRCA1/2* mutation status would increase the SLN involvement rate and have a prognostic impact on breast cancer patients treated with SLN biopsy. Therefore, it remains debatable whether SLN biopsy, the current surgical management strategy of choice for axilla staging, is a safe and rational option for clinically node-negative breast cancer patients with germline *BRCA1/2* mutations, especially in the Chinese population.

In this study, we enrolled breast cancer patients from the *BRCA1/2* germline screening databases who were clinically node-negative on the first presentation and who received SLNB. We aim to investigate the association between the clinicopathological characteristics of patients, including *BRCA1/2* mutation status, SLN involvement rate, and

patient prognosis.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-5996).

Methods

Ethics

All the procedures performed in this study involving human participants were conducted following the ethical standards of the institutional and national research committees and with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Peking Union Medical College Hospital (No. ZS 1655), and written informed consent was retrieved from all participants.

Study design and participants

Between January 2016 and April 2020, clinically node-negative primary breast cancer patients treated with conventional surgery from Peking Union Medical College Hospital and the Cancer Hospital of the Chinese Academy of Medical Sciences were retrospectively screened for *BRCA1/2* germline mutations according to *BRCA1/2* mutation test criteria. All patients who underwent initial SLNB were selected for this study. Among these, ALND was performed if micrometastases or macrometastases of SLNs were detected. Patients with a diagnosis of another malignant tumor and patients with simultaneous bilateral breast cancer were excluded from this cohort. The inclusion criteria were: (I) confirmed *BRCA1/2* mutation status; (II) clinically node-negative primary breast cancer; (III) received initial SLNB. We excluded patients with a diagnosis of other malignant tumors, including gastric carcinoma, cervical carcinoma, or thyroid carcinoma, and simultaneous bilateral breast cancer.

Breast cancer patients were distributed to groups according to their *BRCA1/2* mutation status and were classified as either *BRCA1/2* mutation carriers or non-carriers. The primary endpoints were SLN involvement rate and breast cancer disease-free survival (DFS). SLN involvement rate was defined as the number of positive lymph nodes divided by the number of all lymph nodes during SLNB.DFS was defined as the first recurrence of the disease at a local, regional, or distant site or the diagnosis of contralateral breast cancer. The secondary endpoint is recurrence-free survival (RFS). The times to these endpoints were calculated from surgery (SLNB) to the first documented event. Breast cancer recurrence is categorized as a locoregional disease (tumors in the breast or ipsilateral supraclavicular, subclavicular, internal mammary, or axillary nodes) (18). Patients with no events were censored at the date of the last follow-up.

BRCA1/2 mutation testing

The criteria for genetic testing of *BRCA1/2* mutation status included (I) triple-negative breast cancer (TNBC) (diagnosed ≤60 years of age); (II) breast cancer diagnosis ≤45 years of age; (III) breast cancer diagnosed at any age with at least one close blood relative with a family history of breast cancer, ovarian carcinoma, male breast cancer, prostate cancer, or pancreatic cancer.

Screening for *BRCA1/2* mutations was performed by analyzing genomic DNA extracted from the patients' peripheral blood and capturing targeted sequences followed by high-throughput sequencing. Quality control of the raw data was performed, followed by the removal of duplicate reads. Clean data were aligned to the hg19 reference genome using variants retrieved by GATK 4.0. ExAC further filtered through the variants and the database of the 1,000 genomes project. The filtered variants included untranslated region variants, intronic variants, splicing variants, and exotic variants. All deleterious mutations were confirmed by Sanger sequencing in duplicate. Pathogenic mutations and probable pathogenic mutations were defined as mutations that lead to a truncated protein or that had previously been reported to be associated with the disease.

Statistical analysis

Categorical variables are presented as frequencies and percentages for clinicopathological characteristics and were analyzed using Pearson's chi-square test, Fisher's exact test, and the continuity correction chi-square test. The univariate Kaplan-Meier method with log-ranking estimates was conducted to produce survival curves and to compare survival outcomes among different patient variables. Variables at or close to a value of $P<0.05$ in the univariate analysis, together with known critical clinical confounders (14,23), were used to perform multivariate Cox regression analysis to compare survival between different *BRCA1/2* mutations. Variables included in the multivariable analysis include age at diagnosis (≤45 and >45 years), tumor

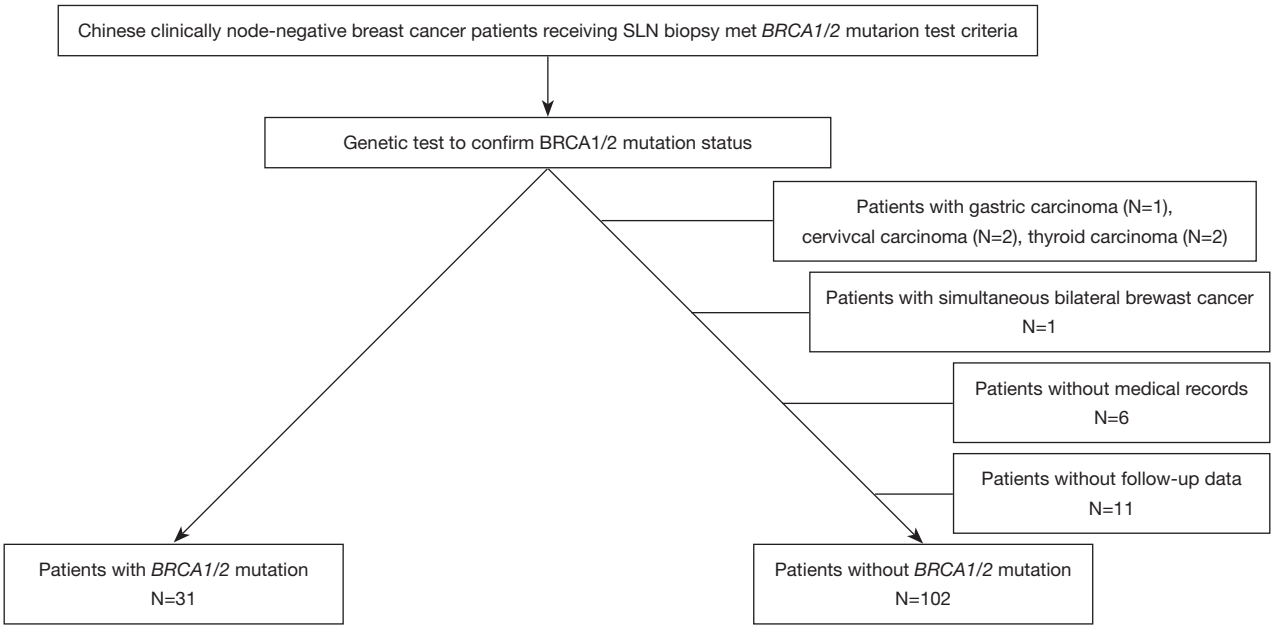

Figure 1 Flow diagram of the patients in the study and analysis.

size (≤2, 2–5, or >5 cm), TNM stage (stage 0, I, II, or III), estrogen receptor (ER) status (positive/negative), and Her-2 status (positive/negative). Systemic treatment for primary breast cancer was considered a variable, with the following categories: chemotherapy (yes/no), endocrine therapy (yes/no) (14), and surgical management of the breast. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

One hundred fifty-six clinically node-negative breast cancer patients underwent the first SLNB and were selected for this study. Of these patients, 31 of them were found as pathogenic *BRCA1/2* germline mutation carriers (19.8%). These included 14 patients with a *BRCA1* mutation (8.9%), 16 patients (10.3%) with a *BRCA2* mutation, and one patient (0.6%) with both *BRCA1* and *BRCA2* mutations. A further 125 patients were classified as non-carriers. Five patients with a diagnosis of other malignant tumors, including gastric carcinoma (n=1), cervical carcinoma (n=2), and thyroid carcinoma (n=2), and one patient with simultaneous bilateral breast cancer were excluded. A further six patients were excluded because of incomplete medical records, and 11 subjects were lost to follow-up. 31 *BRCA1/2* mutation carriers and 102 non-carriers were analyzed in the final cohort (*Figure 1*).

The analysis of clinicopathological characteristics according to the *BRCA1/2* mutation status is shown in *Table 1*. *BRCA1/2* mutation did not increase the SLN involvement rate for clinically node-negative breast cancer patients. This was because we did not observe a significant difference related to surgical management of the axilla, as 19.4% (6/31) of carriers had positive SLNs compared to 16.7% (17/102) of non-carriers (P=0.73). That meant that 6 (19.4%) carriers received ALND followed by SLNB, compared to 17 non-carriers (16.7%). The carrier group proved a tendency towards a slightly younger age than did the non-carrier group, although this difference was insignificant (P=0.38). Twenty-three carriers (74.2%) and 67 non-carriers (65.7%) were under 45 years of age when diagnosed with breast cancer. Interestingly, stage 0 and stage I were more frequent in the carrier group than in the non-carrier group (87.1% versus 59.8%, P<0.01), while stage II and III were more often present in non-carriers than in carriers (40.2% versus 12.9%, P<0.01). There is no significant difference in tumor size, histological type, estrogen receptor (ER) status, progesterone receptor (PR) status, and human epidermal growth factor receptor 2 (Her-2) status. The distribution of systemic therapy was similar between the two groups, including chemotherapy (P=0.19), radiotherapy (P= 0.64), and endocrine therapy (P=0.31).

Table 1 The clinicopathological characteristics of patients receiving SLNB at first according to *BRCA1/2* status

Characteristics	Non-carriers (%) (N=102)	Carriers (%) (N=31)	Total (N=133)	P value
Age				0.38
≤45	67 (65.7)	23 (74.2)	90 (67.7)	
>45	35 (34.3)	8 (25.8)	43 (32.3)	
Tumor size, cm				1.00
≤2	68 (66.7)	21 (67.7)	89 (68.0)	
2–5	32 (31.3)	10 (32.3)	42 (31.5)	
>5	2 (2.0)	0 (0.0)	2 (1.5)	
Histological type				0.44
IDC	88 (86.3)	29 (93.5)	117 (88.0)	
Other	14 (13.7)	2 (6.5)	16 (12.0)	
Number of positive LNs				0.63
0	85 (83.3)	25 (80.6)	110 (82.7)	
1–3	12 (11.8)	3 (9.7)	15 (11.3)	
4–9	3 (2.9)	2 (6.5)	5 (3.8)	
>9	2 (2.0)	1 (3.2)	3 (2.3)	
TNM stage				<0.01
0/I	61 (59.8)	27 (87.1)	88 (66.2)	
II	36 (35.3)	1 (3.2)	37 (27.8)	
III	5 (4.9)	3 (9.7)	8 (6.0)	
ER status				0.59
Positive	47 (46.1)	16 (51.6)	57 (42.9)	
Negative	55 (53.9)	15 (48.4)	70 (57.6)	
PR status				0.26
Positive	41 (40.2)	16 (50.0)	57 (42.9)	
Negative	61 (59.8)	15 (48.4)	76 (57.1)	
HER-2 status				0.95
Positive	9 (8.9)	2 (6.5)	11 (8.3)	
Negative	92 (91.1)	29 (93.5)	121 (91.7)	
Surgical management (breast)				0.48
Breast conserving surgery + RT	60 (58.8)	16 (51.6)	76 (57.1)	
Mastectomy +/– RT	42 (41.2)	15 (48.4)	57 (43.9)	
Surgical management (axilla) (SLN involvement rate)				0.73
SLNB	85 (83.3)	25 (80.6)	110 (82.7)	
SLNB followed by ALND	17 (16.7)	6 (19.4)	23 (17.3)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Non-carriers (%) (N=102)	Carriers (%) (N=31)	Total (N=133)	P value
(Neo) adjuvant chemotherapy				0.19
No	27 (26.5)	7 (14.6)	34 (22.7)	
Yes	75 (73.5)	41 (85.4)	116 (77.3)	
Postoperative radiotherapy				0.64
No	27 (26.5)	4 (12.9)	31 (23.3)	
Yes	75 (73.5)	27 (87.1)	102 (76.7)	
Endocrine therapy				0.31
No	60 (58.8)	15 (48.4)	75 (56.4)	
Yes	42 (41.2)	16 (51.6)	58 (43.6)	

P values were derived from Pearson's Chi-square test, Fisher's exact test, and Continuity Correction chi-square test. IDC, invasive ductal carcinoma; RT, radiotherapy; ER, estrogen receptor; PR, progesterone receptor; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; SLN involvement rate, defined as the number of positive lymph nodes divided by the number of all lymph nodes during SLNB.

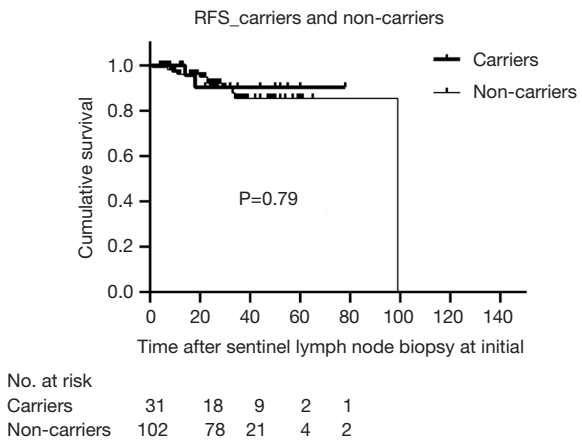

Figure 2 Recurrence-free survival after the first sentinel lymph node biopsy estimated by *BRCA1/2* mutation status in univariate analysis. RFS, recurrence-free survival.

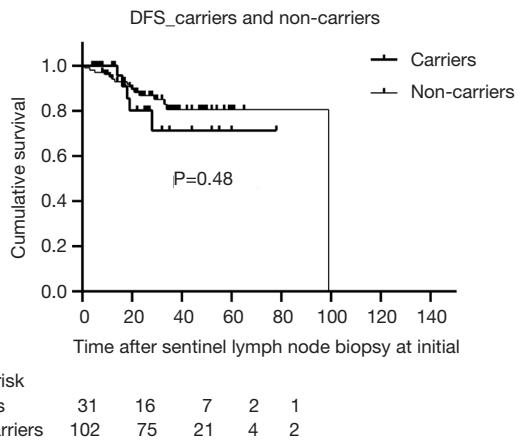

Figure 3 Breast cancer disease-free survival after the first sentinel lymph node biopsy estimated by *BRCA1/2* mutation status in univariate analysis. DFS, breast cancer disease-free survival.

The median duration of follow-up for all patients was 28 months (range, 4–126 months), and 7.1% of patients were lost to follow-up. The RFS of carriers was like non-carriers (P=0.79) (*Figure 2*). In addition, there was no significant difference in DFS between the two groups (P=0.48) (*Figure 3*). For clinically node-negative patients who underwent SLNB at initial presentation, RFS was comparable between carriers and non-carriers [hazard ratio (HR) =0.82; 95% confidence interval (CI): 0.18–3.74; P=0.80]. After adjustment for age, tumor size, and TNM stage, the rate of RFS remained similar between groups (HR =0.89; 95% CI: 0.17–4.63; P=0.89). Likewise, differences in the HRs for RFS remained nonsignificant after additional adjustment for ER and Her-2 status (HR =0.86; 95% CI: 0.17–4.29; P=0.85) and for systemic treatment (HR =0.70; 95% CI: 0.14–3.52; P=0.66) (*Table 2*). After adjustment for surgical management of the breast, there was still no significant difference between the groups in RFS (HR =0.75; 95% CI: 0.14–3.89; P=0.73).

Although the results for DFS were in line with those for

Table 2 Hazard ratios for recurrence-free survival by BRCA1/2 mutation status (N=133)

BRCA1/2 mutation status	*HR (95% CI)	P	†HR (95% CI)	P	‡HR (95% CI)	P	※HR (95% CI)	P	#HR (95% CI)	P
Non-carriers	1.00		1.00		1.00		1.00		1.00	
Carriers	0.82 (0.18–3.74)	0.80	0.89 (0.17–4.63)	0.89	0.86 (0.17–4.29)	0.85	0.70 (0.14–3.52)	0.66	0.75 (0.14–3.89)	0.73

*HR, unadjusted hazard ratio; †HR, hazard ratio adjusted for age, tumor size, and TNM stage; ‡HR, additionally adjusted for ER and Her-2; ※HR, added adjustment for chemotherapy and endocrine therapy; #HR, additional adjustment for surgical management of breast. CI, confidence interval; HR, hazard ratio; ER, estrogen receptor; Her-2, human epidermal growth factor 2.

Table 3 Hazard ratios for breast cancer disease-free survival by BRCA1/2 mutation status (N=133)

BRCA1/2 mutation status	*HR (95% CI)	P	†HR (95% CI)	P	‡HR (95% CI)	P	※HR (95% CI)	P	#HR (95% CI)	P
Non-carriers	1.00		1.00		1.00		1.00		1.00	
Carriers	1.44 (0.52–3.97)	0.48	1.77 (0.54–5.81)	0.34	1.83 (0.57–5.82)	0.30	1.49 (0.45–4.97)	0.51	1.63 (0.48–5.54)	0.43

*HR, unadjusted hazard ratio; †HR, hazard ratio adjusted for age, tumor size, and TNM stage; ‡HR, additionally adjusted for ER and Her-2; ※HR, added adjustment for chemotherapy and endocrine therapy; #HR, additional adjustment for surgical management of breast. CI, confidence interval; HR, hazard ratio; ER, estrogen receptor; Her-2, human epidermal growth factor 2.

RFS (*Table 3*), some differences were observed. The HRs for breast cancer DFS are non-significantly higher both in the unadjusted analysis (HR =1.44; 95% CI: 0.52–3.97; P=0.48) and after adjustment for age, tumor size, and TNM stage (HR =1.77; 95% CI: 0.54–5.81; P=0.34). A similar pattern was observed upon added adjustment for ER and Her-2 status (HR =1.83; 95% CI: 0.57–5.82; P=0.30). Patients with *BRCA1/2* mutations also showed a trend towards worse survival outcomes compared to non-carriers after adjustment for systemic therapy (HR =1.49; 95% CI: 0.45–4.97; P=0.51) and surgical management of the breast (HR =1.63; 95% CI: 0.48–5.54; P=0.43), although this did not reach the level of significance.

Discussion

SLNB has become the standard of care for primary treatment of early breast cancer, replacing ALND for clinically node-negative patients. However, many unresolved issues remain (22), which will still affect the decision-making of SLNB for clinically node-negative patients. Our study showed that *BRCA1/2* mutation status did not increase the SLN involvement rate for the diagnosis of patients with clinically negative nodes (P=0.73); therefore, *BRCA1/2* mutation cannot be used to prevent SLNB during the initial decision-making process. Several factors (22,24) increasing the SLN involvement rate still could affect the decision-making of SLNB for clinically node-negative breast cancer patients, including tumor size (25), multiple foci (26), imaging examination (27,28), and others. Completion ALND will be applied if SLN involved those factors that may bring unnecessary cALND with an increasing SLN involvement rate. So far, Giammarile *et al.* (29) suggested that axillary recurrence was associated with larger tumors. Simultaneously, Spillane *et al.* (30) reported that the identification rate for multiple breast cancers was like unifocal tumors, although there was a higher rate of positive SLN.

The false negative rate (FNR) of SLNB, different from the SLN involvement rate, is defined by doing a sentinel-node biopsy followed by a back-up axillary dissection to determine if there were additional positive nodes in the axillary dissection that were not seen on sentinel node biopsy (31). Krag *et al.* (32) reported that the SLNB technique is associated with a false negative rate of 5% to 10%. Several factors were reported increasing FNR of SLNB such as neoadjuvant chemotherapy (33) and mapping methods for SLNB (34). For the former, the FNR might be controlled through IHC staining combined with H&E staining for SLN and increasing the total numbers of SLN (17). For the latter, combination of two mapping methods for SLNB at least might take work including the use of blue dye tracer (e.g., isosulfan blue, methylene blue, and patent blue dye), use of radioisotope tracer, and use

of indocyanine green (34). However, none of these earlier investigations have considered *BRCA1/2* mutation status as a factor increasing FNR of SLNB. Further research may be designed investigating whether *BRCA1/2* mutation status could increase the FNR of SLNB through comparing FNR between patients with or without *BRCA1/2* mutation however in which all the patients should receive initial SLNB then followed by ALND. It is unrealistic and lake of operability in which SLNB was approved safely. In addition, those ways decreasing the FNR of SLNB still can be used for the *BRCA* carriers. Thus, To the best of our knowledge, it is enough to investigate the effect of *BRCA1/2* mutation status on the SLN involvement rate for clinical node-negative breast cancer so that *BRCA1/2* mutation will not affect the decision making of SLNB.

To enhance our findings, we also showed the prognostic impact of *BRCA1/2* mutation status on the initial SLNB. DFS was comparable between carriers and non-carriers (P=0.48), findings that did not change after adjustment for clinicopathological characteristics, systemic treatment and surgical management of the breast (BCT versus mastectomy) (HR =1.63; 95% CI: 0.48–5.54; P=0.43). These results were consistent with those of the Z0011 trial, which also used DFS as the study endpoint (18). Additionally, RFS was in line between the groups (P=0.79). After adjustment for clinicopathological characteristics, and systemic treatment, it was still in line (HR =0.70; 95% CI: 0.14–3.53; P=0.66). Considering surgical management of the breast (BCT versus mastectomy) was an important confounding factor, it has been added into adjustment (HR =0.75; 95% CI: 0.14–3.89; P=0.73). These results were also in correspondence with the findings of the Dutch Randomized Controlled Multicenter Trial (BOOG 2013-08) as using RFS as the study endpoint (35). They reported that the 5-year regional RFS rate of SLNB was significantly non-inferior to ALND (99% versus 96%) for women with clinically node-negative T1–2 invasive breast cancer.

Both for non-adjusted and adjusted RFS and DFS, the carrier group HRs are below 1.0 for RFS but above 1.0 for DFS. These results were observed conversely to there being no significant differences between the groups. DFS events included metastasis and contralateral breast cancer; therefore, the difference in HRs between RFS and DFS might be because of the increased risk of contralateral breast cancer in carriers. These findings are supported by the findings of Kuchenbaecker *et al.* (36), who reported the risk of contralateral breast cancer increased in *BRCA1/2* mutation carriers, especially among patients who carried the *BRCA1* mutation.

We include different surgical management of the breast (BCT versus mastectomy) into adjusted analysis for the prognostic impact of *BRCA1/2* mutations on SLNB. Surgical management related to breast cancer involves both breasts and axillae. *BRCA1/2* mutation increased the risk of cancer in the breast; therefore, previous studies investigated whether *BRCA1/2* mutations would affect the prognosis when different surgical management of breast (BCT *vs.* mastectomy) (14,37,38). Thus, in this study, different surgical management of breast was adjusted as an independent confounding factor for RFS and DFS so that both RFS and DFS would not be affected. Thus, it was necessary to consider whether different surgical management of breasts in the adjusted analysis for both RFS and DFS, especially for the former.

Although this is the first study to conclude that *BRCA1/2* mutation does not increase involved SLN rate of initial SLNB or affect the prognosis of clinically node-negative breast cancer patients receiving initial SLNB, the study has limitations. The follow-up duration was insufficient. The small sample size and insufficient stratification by *BRCA1* and *BRCA2* mutation types are added limitations of this study. Even though, due to similar mechanism of both *BRCA1* and *BRCA2* in a common pathway of genome protection (39) and low frequency of *BRCA1* or *BRCA2* mutation (23), several studies (13,23) were still investigated without stratification by *BRCA1* or *BRCA2* mutation types. Only female patients were included for analysis. Thus, the findings may be applicable only for Chinese female patients with clinically node-negative breast cancer with *BRCA1/2* mutations. Although the sample size is small, this is still exploratory research that can serve as the basis for prospective research.

Conclusions

In summary, this study suggests that *BRCA1/2* mutations do not increase the SLN involvement rate of the initial SLNB. RFS and DFS for *BRCA1/2* mutation carriers among Chinese women are equivalent to those of non-carriers. Thus, SLNB should be considered for clinically node-negative breast cancer regardless of *BRCA1/2* status

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Footnote

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