Hereditary Breast Cancer

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Minoru Miyashita and Takanori Ishida

Abstracts

In hereditary breast cancer, the different strategies from sporadic cancer might be required due to its vulnerable feature. We reviewed the published data of breast cancers with germline BRCA1/BRCA2, TP53, PTEN, CDH1, PALB2, CHEK2, ATM, and STK11 focusing on the treatment. The standard of locoregional treatment including surgery and radiation therapy (RT) should be considered in hereditary breast cancer except for TP53-related breast cancer as in sporadic breast cancer. Mastectomy is recommended without RT for germline TP53 mutation carriers. Because there is a lack of reliable data about treatment of hereditary breast cancer, the discussion about the risk of both recurrence and new breast cancer is encouraged. Chemotherapy including platinum is recommended for metastatic breast cancer with BRCA1/BRCA2 mutation. However, there is no data supporting the use of platinum in (neo)adjuvant settings for early breast cancer with BRCA1/BRCA2 mutation. More researches about treatment for hereditary breast cancer are considered indispensable.

Keywords

Hereditary breast cancer · BRCA1/BRCA2 · TP53 · PTEN · CDH1 · PALB2 · CHEK2 · ATM · STK11

M. Miyashita (✉) · T. Ishida
Departments of Breast and Endocrine Surgical Oncology, Tohoku University Graduate School of Medicine, Sendai, Japan
e-mail: atihsayim8m8@med.tohoku.ac.jp; takanori@med.tohoku.ac.jp

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6.1 Introduction

Breast cancer is one of the most important health problems for women throughout the world, reporting woman's lifetime risk of developing breast cancer at 1 in 8. About 5% to 10% of breast cancer cases are thought to be hereditary so that the multidisciplinary approach is demanded. Because of the vulnerable feature of hereditary breast cancer, the different strategies from sporadic cancer might be required. Here, we reviewed the published data of breast cancers with germline BRCA1/BRCA2, TP53, PTEN, CDH1, PALB2, CHEK2, ATM, and STK11 focusing on the treatment.

6.2 BRCA1-/BRCA2-Related Breast Cancer

The rate of germline BRCA1/BRCA2 mutations in all patients with breast cancer is around 4% [1, 2], and the incidences are particularly higher in patients with triple-negative breast cancer and Jewish women with breast cancer which are around 15% in both populations [3–5]. The prognostic risk is reported to vary based on the objective population [6, 7]. According to the study which included Japanese female breast cancer having strong family history of breast cancer based on the NCCN guidelines, the rates of germline BRCA1 and BRCA2 mutations among 260 breast cancer are 17.7% and 13.5%, respectively [8] (Fig. 6.1).

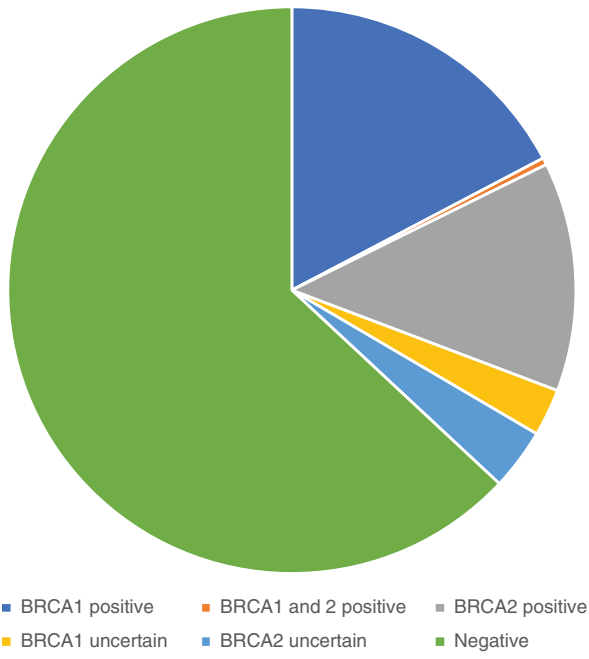

Fig. 6.1 Result of BRCA1/BRCA2 genetic testing of 260 Japanese female breast cancer having strong family history of breast cancer based on the NCCN guidelines. Modified from [8]

Treatment decisions for BRCA1-/BRCA2-related breast cancer might be influenced by the genetic instability. Here, we comprehensively reviewed the treatments and prognosis of breast cancer with BRCA1/BRCA2 mutation carriers. We refrained from describing about therapeutic endocrine therapy because of the lack of evidence.

6.3 What Is the Appropriate Surgical Management for BRCA1-/BRCA2-Related Breast Cancer?

6.3.1 Breast Conserving Surgery or Mastectomy

One of the clinical questions we need to address is whether or not breast conserving surgery (BCS) is safe for BRCA1/BRCA2 mutation carriers as a part of treatment because of the higher incidence of breast cancer. Van den Broek AJ, et al. evaluated the effects comparing among BCS by radiotherapy, mastectomy without radiotherapy, and mastectomy followed by radiotherapy in terms of overall and breast cancer-specific survival as well as local recurrence rates and ipsilateral new primary breast cancer [9]. After adjusting the confounders affecting the treatment choice, both BRCA1 mutation carriers ($N = 191$) and non-carriers ($N = 5820$) had a similar overall survival regardless of the type pf local treatment, BCS or mastectomy. In their study, numbers for BRCA2 mutation carriers ($N = 70$) were insufficient to reach conclusions. Interestingly, the 10-year risk of local recurrence rates after BCS did not differ between BRCA1 mutation carriers and non-carriers (7.3% and 7.9%, respectively). In contrast, Nilsson MP, et al. reported the increment of local recurrence rates in BRCA1/BRCA2 mutation carriers receiving BCS. They investigated local recurrence and overall survival of BRCA1/BRCA2 mutation carriers in the comparison between BCS ($N = 45$) and mastectomy ($N = 118$) [10]. The cumulative local recurrence risk in 5, 10, and 15 years was 15%, 25%, and 32% in patients with BCS although it was 9% throughout 15 years in patients with mastectomy. No significant difference of distant recurrence or overall survival between the groups was observed. As the largest study, Pierce LJ, et al. examined long-term outcome of 655 breast cancer patients with BRCA1/BRCA2 mutation. Cumulative local recurrence rate in 15 years was significantly higher in patients who underwent BCS compared to mastectomy, 23.5 vs. 5.5%, respectively [11]. There were no differences in both distant recurrences and overall survival between two groups.

Throughout the literature review of this clinical question, BCS is considered to be feasible in breast cancer with BRCA1/BRCA2 mutation carriers based on the survival data. However, discussion about the increasing risk of local recurrence is mandatory between patients and physicians. No randomized control trial exists so that we have to make a clinical decision following the observational studies having the selection bias.

6.3.2 Nipple-Sparing Mastectomy

Nowadays, nipple-sparing mastectomy (NSM) is widely performed with breast reconstruction. A few studies examined the option of NSM for breast cancer patients with BRCA1/BRCA2 mutation carriers. Yao K, et al. retrospectively analyzed the clinical data of BRCA1/BRCA2 mutation carriers ($N = 51$) who underwent NSM for newly diagnosed breast cancer [12]. Three patients experienced the cancer events including one patient with local and distant recurrence and two patients with axillary recurrences. There was no patient with BRCA1/BRCA2 mutation who had a recurrence at the nipple-areolar complex.

Manning AT, et al. identified 26 breast cancer patients with BRCA1/BRCA2 mutation who underwent NSM, while analyzing details of patient demographics, surgical procedures, complications, and relevant disease stage and follow-up [13]. There was no event of local recurrence and two cancer-related deaths were observed; one patient had distant metastases after NSM and another patient had ovarian cancer after NSM for DCIS.

In the field of therapeutic NSM in BRCA1/BRCA2 mutation carrier, limited reports are available to the best of our knowledge. Although the mentioned studies suggested the acceptable rates of local recurrence after NSM, the median follow-up period was not enough: 32.6 months in the study of Yao K, et al. and 28 months in the study of Manning AT, et al. The safety of therapeutic NSM in BRCA1/BRCA2 mutation carrier remains unclear due to the unavailability of the reliable data with larger sample size and longer follow-up time. Shared decision making with clinicopathological factors and patients' preference should be thoroughly done for the optional surgical procedure.

6.3.3 Contralateral Risk-Reducing Mastectomy

High risk of contralateral event is well known among breast cancer patients with BRCA1/BRCA2 mutation. For these women, contralateral risk-reducing mastectomy (CRRM) decreases the newly diagnosed contralateral breast cancer, whereas whether CRRM improves overall survival needs to be clarified. Heemskerk-Gerritsen BAM, et al. evaluated the role of CRRM on survival in BRCA1/BRCA2 mutation carriers with a history of primary breast cancer [14]. Out of patients receiving CRRM ($N = 242$), 4 patients developed contralateral breast cancer (2%) with the median follow-up period of 11.4 years after primary breast cancer, which was fewer than 64 patients (19%) out of the surveillance group ($N = 341$). The mortality was also lower in the CRRM group than in the surveillance group (9.6 and 21.6 per 1000 person-years of observation, respectively).

Metcafe K, et al. studied 390 BRCA1/BRCA2 mutations carriers with stage I or II breast cancer including 181 patients who had CRRM [15]. In the median follow-up time of 14.3 years, 18 women died in the CRRM group and 61 in the unilateral mastectomy group.

The survival rates at 20 years were 88% and 66% in the CRRM and the unilateral mastectomy group, respectively. In a multivariable analysis, CRRM was significantly associated with a 48% reduction in breast cancer death. Soenderstrup IM, et al. analyzed 237 breast cancer patients with BRCA1/BRCA2 mutation according to the types of surgery, treatments, and characteristics [16]. The results showed that CRRM was associated with reduced risk of death, but not with disease-free survival. Evans DG, et al. investigated the impact of CRRM on survival in unilateral breast cancer with BRCA1/BRCA2 mutations [17]. In a matched case–control analysis designed to control for potential confounding factors (BPO, stage, and tumor characteristics), overall survival in the 105 CRRM cases was significantly higher, which was 89% versus 73% in 105 controls who did not have CRRM.

Contrary, Van Sprundel TC et al., reported the opposite result that CRRM for 79 breast cancer patients with BRCA1/BRCA2 mutation reduced the risk of contralateral breast cancer by 91%. At 5-year follow-up, overall survival was 94% for the CRRM group against with 77% for the surveillance group. After adjustment for bilateral prophylactic oophorectomy (BPO) in a multivariate analysis, however, CRRM was not significantly prognostic for overall survival.

Overall, CRRM clearly decreases the incidence of contralateral breast cancer in BRCA1/BRCA2 mutation carriers, whereas the benefit of CRRM for survival differs among the studies and the analytic methods. There is insufficient evidence we can utilize whether CRRM improves survival so that various factors around patients should be taken into consideration to decide the indication of CRRM for BRCA1/BRCA2 mutation carriers having a history of unilateral breast cancer.

6.4 Can RT Be Recommended for BRCA1-/BRCA2-Related Breast Cancer?

6.4.1 Breast Radiation After BCS

To plan a series of treatment for women with BRCA1-/BRCA2-related breast cancer, revealing the benefit and the risk of RT is necessary. The meta-analysis including ten studies which investigated the safety of RT after BCS in breast cancer patients with BRCA1/BRCA2 mutation was conducted by Valachis A, et al. [18]. The results suggested no significant difference between carriers and controls in terms of ipsilateral breast recurrence, which was 17.3% in BRCA1/BRCA2 mutation carriers and 11.0% in non-carriers (RR 1.45, 95% CI 0.98–2.14). Additionally, use of adjuvant chemotherapy and oophorectomy decreased the incidence of ipsilateral breast recurrence for BRCA mutation carriers. However, a significant higher risk for IBR in BRCA mutation carriers was observed when only studies with a median follow-up of 7 years were analyzed (RR 1.51, 95% CI 1.15–1.98). Therefore, further follow-up time is required. RT after BCS can be considered as a reasonable option and should not be withheld only due to mutation status based on the currently available evidence.

6.4.2 Postmastectomy Radiation Therapy

Limited studies reported the data about the efficacy of postmastectomy radiation therapy (PMRT) in BRCA1/BRCA2 mutation carriers. Pierce LJ, et al. compared the local recurrence rates of patients with mastectomy and PMRT ($N = 103$) with that of patients with mastectomy only ($N = 250$) among BRCA1/BRCA2 mutation carriers [11]. Despite higher stage among with PMRT, the local recurrence rates were similar between two groups. Median time to local failure was 9.4 years for patients with mastectomy. Drooger JC, et al. performed multivariate analysis of the subgroups under 40 ages as a part of entire cohort of BRCA1/BRCA2 mutation carriers [19]. The risk of contralateral breast cancer did not differ among groups, RT after BCS, RT after mastectomy, and mastectomy alone. In this study, ipsilateral local recurrence after mastectomy was not evaluated. The decision regarding PMRT should not be based predominantly on BRCA1/BRCA2 mutation status.

6.4.3 RT-Related Toxicity

By the time we searched, three studies were reported about their investigation about RT-related toxicity in breast cancer patients with BRCA1/BRCA2 mutations. Pierce LJ, et al. reported no differences about the incidence rates of chronic skin, subcutaneous tissue, lung, or bone complications between BRCA1/BRCA2 mutation carriers ($N = 71$) and sporadic cohorts ($N = 213$) [20]. Park H, et al. also reported no increased risk in acute skin toxicity in BRCA1/BRCA2 mutation carriers ($N = 46$) receiving BCS and RT compared with women with sporadic breast cancer [21]. Shanley S, et al. reported the similar finding about acute and late radiation effects between BRCA1/BRCA2 mutation carriers ($N = 55$) and sporadic breast cancer ($N = 55$) in a matched case–control study of patients treated with RT [22]. Although further studies are required to identify genetic effects to normal tissue responses after RT, there is no evidence of a significant increase of RT-related toxicity among breast cancer patients with BRCA1/BRCA2 mutation.

6.5 What Is the Role of Chemotherapy (Platinum) for BRCA1-/BRCA2-Related Breast Cancer?

6.5.1 Early Breast Cancer

Although several studies investigated the efficacy of platinum for early breast cancer (EBC) with BRCA1/BRCA2 mutation in (neo)adjuvant settings, there are only two randomized controlled trials. The exploratory analysis of 50 BRCA1/BRCA2 mutation carriers from GeparSixto trial was reported by Hahnen E, et al. [23]. The pathological complete response (pCR) rate was 66.7% (16 of 24) for BRCA1/

BRCA2 mutation carriers and 36.4% (44 of 121) for non-carrier patients (OR, 3.50; 95% CI, 1.39–8.84; $P = 0.008$) without carboplatin. However, the addition of carboplatin to the neoadjuvant chemotherapy regimen did not increase the pCR rate of BRCA1/BRCA2 mutation carriers (17 of 26 [65.4%]). Disease-free survival of patients with BRCA1/BRCA2 mutation carriers did not differ between the treatment regimens with and without carboplatin. Loibl S, et al. performed the subgroup analysis of 92 BRCA1/BRCA2 mutation carriers from BrighTNess trial [24]. Overall, the pCR rate was 51% (47 of 92 patients) with BRCA1/BRCA2 mutation carriers and similar with that of non-carrier patients, 48% (262 of 542). The pCR rates of each regimen in BRCA1/BRCA2 mutation carriers were 57% (26 of 46), 50% (12 of 24), and 41% (9 of 22) in paclitaxel + carboplatin + veliparib group, paclitaxel + carboplatin group, and paclitaxel group, respectively. Although adding carboplatin increased the pCR rate to some degree, the stratified analysis showed that additive benefit of carboplatin was observed for non-carrier patients rather than BRCA1/BRCA2 mutation carriers.

The meta-analysis including non-randomized controlled trial indicated that 93 of 159 (58.4%) patients with BRCA1/BRCA2 mutation achieved pCR, while 410 of 808 (50.7%) with non-carrier patients by the platinum-containing regimens [25]. The result did not show statistical significance (OR 1.459 CI 95% [0.953–2.34] $P = 0.082$). As shown, platinum to current standard regimens of anthracycline and taxane is not recommended as the routine addition for breast cancer patients with germline BRCA mutation.

6.5.2 Metastatic Breast Cancer

Two prospective studies addressed the efficacy of platinum in metastatic breast cancer patients who have BRCA1/BRCA2 mutation. Tutt A, et al. reported the result of TNT trial which evaluated the efficacy of two single-agent chemotherapies, carboplatin or docetaxel, in metastatic TNBC [26]. In the preplanned subject with 43 germline BRCA1/BRCA2 mutated patients from entire cohort, carboplatin had more than double the objective response rate of docetaxel (68% vs. 33%, respectively). Progression-free survival of patients with BRCA1/BRCA2 mutation was longer than that of non-carrier patients (6.8 months vs. 4.4 months, $P = 0.002$). Zhang J, et al. reported the result of CBCSG006 trial which included 14 BRCA1/BRCA2 mutation carriers [27]. Patients with germline BRCA1/BRCA2 mutation had suggestively higher objective response rate by cisplatin-containing regimen (83.3% in cisplatin plus gemcitabine group vs. 37.5% in paclitaxel plus gemcitabine group, $P = 0.086$). Cisplatin plus gemcitabine regimen also prolonged progression-free survival compared to paclitaxel plus gemcitabine regimen (8.9 months vs. 3.2 months, $P = 0.459$). Although there is no randomized controlled trial focusing on only BRCA mutation carriers, platinum could be an optional regimen for metastatic breast cancer patients with BRCA1/BRCA2 mutation.

6.6 BRCA1-/BRCA2-Related Breast Cancer Has Worse Prognosis?

According to the reports from retrospective studies which investigated the prognosis of breast cancer patients with BRCA1/BRCA2 mutation, there are conflicting results of the contribution by the germline mutation. However, Templetion AJ, et al. reported that BRCA mutation of 1325 patients was not associated with worse prognosis by the systematic review which consists of 16 studies comprising 10,180 patients [28].

Two large-scale prospective studies found no clear evidence that germline BRCA1/BRCA2 mutations significantly affect overall survival. Goodwin PJ, et al. conducted an international population-based cohort study of 3220 women with incident breast cancer observed prospectively, which included 93 BRCA1 mutations and 71 BRCA2 mutations: 1, both mutations [29]. With mean follow-up of 7.9 years, distant disease recurrence survival and overall survival did not differ between BRCA1 mutation carriers and non-carriers. Although distant disease recurrence survival and overall survival was worse in BRCA2 mutation carriers compared with non-carriers in univariable analysis, no difference was observed in both endpoints after adjustment for age, tumor stage and grade, nodal status, hormone receptors, and year of diagnosis. Copson ER, et al. performed a prospective cohort study of 2733 breast cancer patients aged 40 years or younger at histological diagnosis of invasive breast cancer [30]. Survival of 338 breast cancer patients with BRCA mutation (201 with BRCA1, 137 with BRCA2) was compared to that of sporadic breast cancer patients within a median follow-up of 8·2 years. The results showed no significant difference in overall survival between BRCA mutation carriers and non-carrier patients in multivariable analysis at any follow-up timepoint. Conversely, triple-negative breast cancer with BRCA mutation had better overall survival than non-carriers at 2 years. However, this better outcome was not observed at 5 and 10 years. Following the high-evidence studies, there was no data showing the worse prognosis of breast cancer with BRCA1/BRCA2 mutation.

6.7 TP53-Related Breast Cancer

TP53 gene is one of the most common tumor suppressors among cancers, providing its function to suppress tumor growth through making a protein p53. Li–Fraumeni syndrome (LFS) related to germline alterations of TP53 causes the early-onset of cancers among adolescent and young adult, especially soft-tissue sarcomas, breast cancers, central nervous system tumors, and so on. Currently, breast cancer with germline TP53 variants is more identified due to the more availability of multigene tests. At the review about germline TP53 variants in breast cancer patients outside the strict clinical criteria for LFS testing, the incidence rate of TP53 carriers was from 0% to 7.7% among the 59 studies [31]. TP53 carrier rate outside LFS was from 3.8% and 7.7% when the tests were performed for selected patients based on early-onset but not family history.

When offering treatments for breast cancer patients with germline TP53 mutation, RT particularly should be paid attention. Because of the function of TP53 gene to repair DNA damage, RT to breast tissue, chest wall, and other region would cause unfavorable effects in breast cancer patients. Heymann S. et al. studied 8 breast cancer patients diagnosed as the first tumor event of LFS among 47 documented Li–Fraumeni families [32]. Median age at the diagnosis was 30 years and six patients had received RT (three for conserving breast and three for chest wall). With median follow-up of 6 years, three ipsilateral breast recurrences, three contralateral breast cancers, two radio-induced cancers, and three new primaries (one of which was an in-field thyroid cancer with atypical histology) were diagnosed among six patients receiving RT. Other case reports suggested the unfavorable outcomes of TP53-related breast cancers as well [33–35]. Based on the current available data, BCS and RT for breast tissue should not be indicated for breast cancer patients with germline TP53 mutation. Although an alternative option does not exist except mastectomy, PMRT should be considered only in patients with higher risk of recurrence.

6.8 PTEN-Related Breast Cancer

PTEN gene is known as a tumor suppressor which produces the enzyme regulating cancer cells in various ways. Among hereditary breast cancer, Cowden syndrome (CS) is well known as a germline PTEN mutation causing multi-system disorder including malignant tumors of the breast, endometrium, thyroid, and so on. The lifetime risk of breast cancer associated with a mutation in PTEN is estimated from 77% to 85% for women [36, 37]. Unfortunately, there are few reports about what treatment is recommended for women with PTEN-related breast cancer. The only thing we could mention is that breast cancer patients with germline PTEN mutation are at increased risk of not only second breast cancer but endometrial, thyroid, renal, and colorectal cancers. Therefore, the active screening and prophylactic surgery could be considered. Even if breast cancer patients without germline PTEN mutation meet the CS diagnostic criteria, a comprehensive approach to those women is necessary as well as mutation carriers [38].

6.9 CDH1-Related Breast Cancer

CDH1 gene provides a protein E-cadherin which functions as an adhesion factor in the cell membrane and characterizes especially the morphological feature of lobular breast cancer (LBC). Hereditary invasive lobular breast-diffuse gastric cancer related to germline CDH1 mutations is one of the genetically high-penetration breast cancers. The International Gastric Cancer Linkage Consortium reported that the estimated risk for diffuse gastric cancer was from 67% to 83% [39, 40]. On the other hand, the estimated risk for LBC was around 40% by age 80 years. Corso G, et al. reported the results of their literature review which included 483 IBCs from 9 studies outside the pedigrees of diffuse gastric cancer [41]. Mean age at the

diagnosis of LBC was 46 years. Out of 483 patients, 14 novel deleterious alterations (2.9%) have been reported. Apart from prophylactic surgery, appropriate management of surgery and RT remains unclear. The clinical decision should be made taking into account the various factors, like the extent of tumor, the quality of imaging, the preference of patient, and so on.

6.10 PALB2-Related Breast Cancer

PALB2 gene encodes a protein which helps genome maintenance, especially double-strand break repair of BRCA2. While biallelic germline mutation (loss-of-function) in PALB2 is related to the onset of Fanconi's anemia, monoallelic mutations (loss-of-function) increase the risk of breast cancer and pancreatic cancer [42]. Antoniou AC, et al. analyzed the information of 362 members in 154 families who had deleterious PALB2 mutations [43, 44]. The estimated absolute risks of breast cancer for PALB2 mutation carriers were 33% and 58% for those without and with family history of breast cancer. Cybulski C, et al. reported the result of their retrospective study to evaluate the incidence rate of mutation and prognosis [45]. Out of 12,529 women with breast cancer, 116 patients (0.93%) were detected as the PALB2 mutation carriers. As controls, 10 participants were positive of PALB2 mutation in 4730 women who were free from cancer. The authors suggested that breast cancer patients with PALB2 mutations had worse prognosis than non-carrier patients. However, the adjustment of variable seems not to be done thoroughly. In this study, the 5-year cumulative incidence of contralateral breast cancer was reported to be 10% in PALB2 mutation carriers. Although the appropriate therapeutic approach for breast cancer patients with PALB2 mutation is unclear, the standard management should not be withheld for the reason of germline mutation in PALB2.

6.11 CHEK2-Related Breast Cancer

CHEK2 gene is one of tumor suppressors among cancers, providing its function to induce cell death through producing a protein CHK2. CHEK2 (1100delC) is generally classified into moderate risk category and the lifetime risk is estimated from 25% to 30% [46]. Lee A, et al. newly proposed the risk prediction model of hereditary breast cancer using both genetic and non-genetic risk factors [47]. Based on their risk mode, the cumulative incidence of breast cancer among CHEK2 mutation carriers varied from 20% to 35% depending on the questionnaire-based risk factors, mammographic density, and polygenic risk scores. Several studies reported the increasing risk of second breast cancer in breast cancer patients with CHEK2 mutation [48–51]. This information of CHEK2 1100delC about the risk of second breast cancer, especially contralateral breast cancer, should be shared when discussing the therapeutic options.

6.12 ATM-Related Breast Cancer

ATM gene codes a protein which is a key regulator of cellular pathways protecting cells from DNA double-strand break. The lifetime risk of breast cancer related to germline ATM mutation is approximately 30% which changes due to the other non-genetic risks [46, 47]. When considering BCS and RT for breast cancer patients with ATM mutation, ipsilateral cancer recurrence and the toxicity of RT need to be taken into account. Meyer A, et al. studied 135 breast cancer patients treated with RT after BCS including 20 ATM mutation carriers [52]. The results showed no significant difference between carriers and non-carriers in terms of local recurrence and metastatic-free survival by multivariate analysis. Regarding the toxicity of RT especially ones related to skin and subcutaneous tissues, the conflict results exist [53–55]. Some studies reported the data about the incidence of CBC after RT to breast tissue in breast cancer patients with ATM mutation.

Bernstein JL, et al. suggested that RT was significantly associated the risk of CBC in breast cancer patients with ATM deleterious missense variant compared to non-carriers [56]. In contrast, the other two studies reported no increase of CBC among breast cancer patients with ATM mutation who received RT after BCS [57, 58]. The evidence on hand is limited so that more research is required. The current practice including BCS and RT should be offered for breast cancer patients with ATM mutation if indicated. The physician also needs to discuss about the toxicity of RT and the potential CBC.

6.13 STK11-Related Breast Cancer

STK11 gene which is sometimes called LKB1 suppresses cell growth by producing the enzyme. The gene is also known to lead to Peutz–Jeghers syndrome (PJS) composing a wide spectrum of cancers, gastrointestinal cancers, breast cancers, ovary cancers, and so on. The cumulative risks of breast cancer in PJS patients are 8%, 13%, 31%, and 45% at the age of 40, 50, 60, and 70 years, respectively [59]. Unfortunately, there was no available data to decide what treatment is indicated for breast cancer patients with STK11 mutation. The standard of care should be offered for the population while discussing the risk caused by STK11 mutation.

6.14 Conclusion

In this field, there are few reliable evidences about treatment of hereditary breast cancer so that we need to discuss about the balance between benefit and risk of treatment, adapting to each patient. More researches about treatment for hereditary breast cancer are considered indispensable.

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