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Breast Cancer Risk Prediction in Korean Women: Review and Perspectives on Personalized Breast Cancer Screening

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ABSTRACT

Due to an increasing proportion of older individuals and the adoption of a westernized lifestyle, the incidence rate of breast cancer is expected to rapidly increase within the next 10 years in Korea. The National Cancer Screening Program (NCSP) of Korea recommends biennial breast cancer screening through mammography for women aged 40–69 years old and according to individual risk and preference for women above 70 years old. There is an ongoing debate on how to most effectively screen for breast cancer, with many proponents of personalized screening, or screening according to individual risk, for women under 70 years old as well. However, to accurately stratify women into risk categories, further study using more refined personalized characteristics, including potentially incorporating a polygenic risk score (PRS), may be needed. While most breast cancer risk prediction models were developed in Western countries, the Korean Breast Cancer Risk Assessment Tool (KoBCRAT) was developed in 2013, and several other risk models have been developed for Asian women specifically. This paper reviews these models compared to commonly used models developed using primarily Caucasian women, namely, the modified Gail, Breast Cancer Surveillance Consortium, Rosner and Colditz, and Tyrer-Cuzick models. In addition, this paper reviews studies in which PRS is included in risk prediction in Asian women. Finally, this paper discusses and explores strategies toward development and implementation of personalized screening for breast cancer in Korea.

Keywords: Breast neoplasms; Early detection of cancer; Precision medicine

INTRODUCTION

In Korea, breast cancer is the most common among all cancers in women. In 2017, there were 22,300 new cases and the crude incidence rate was 86.9 per 100,000, according to data from the Korea National Cancer Incidence Database (KNCID) [1]. The number of incident breast cancers in 2019 was estimated to be at 24,010, with a crude incidence rate of 92.9 per 100,000 [2], suggesting an increasing trend. An epidemiologic study suggests that the incidence rate is expected to rapidly increase within the next 10 years in Korea due to an increasing proportion of older individuals in the population and continuous adoption of the westernized lifestyle [3]. This trend highlights the importance of effective breast cancer screening in Korea.

The National Cancer Screening Program (NCSP) in Korea introduced breast cancer screening in 2002 [4]. As of 2015, the NCSP guideline recommends routine biennial breast cancer screening by mammography for women aged 40–69 years old and for women above 70 years old according to individual preference and risk [5]. This recommendation of NCSP was formed based on several randomized studies in the United States, Scotland, and Sweden that showed 10%–27% mortality rate reduction of breast cancer by mammographic screening for women aged 40–74 years old [6]. This recommendation is somewhat different from those of other countries. For example, in the United States, the U.S. Preventive Services Task Force recommends biennial screening mammography for women 50–74 years with average risk [7]. Other societies in the U.S., including the American College of Radiology and the American Cancer Society, recommend slightly different screening intervals and starting ages [8,9]. Differences between guidelines from different countries or even within the same country seem to be related to different epidemiologic characteristics of breast cancers observed between countries and also by an ongoing debate on the actual effectiveness of mammographic screening in decreasing mortality, along with the issues of overdiagnosis for individuals at low risk and underdiagnosis for individuals at high risk [10,11].

In Korea, the adherence rate to mammography was 63.9% in 2018 [12]. Data from the NCSP showed significant increases in the diagnosis of ductal carcinoma *in situ* (DCIS) and localized breast cancers compared to patients had never been screened (adjusted odds ratio [OR], 1.89; 95% confidence interval [CI], 1.57–2.29). However, the increased screening did not translate into a decrease in regional disease, suggesting the possibility of overdiagnosis [13]. Thus, there is great interest in improving methodologies for breast cancer screening, and the exploration and testing of risk-based screening strategies are actively underway in some countries [14,15].

Risk-based screening has the potential to improve screening guideline adherence, improve screening efficiency, and decrease harms associated with overscreening and overdiagnosis. To implement an effective risk-based screening program in a population, it is necessary to understand the epidemiology, characteristics, and risk distribution of breast cancer within the target population. Most studies on breast cancer, including those informing risk prediction and screening guidelines, have been conducted in Western countries. However, there are differences in epidemiology, characteristics, and risk factors between breast cancer patients in Korea compared to Western countries [16,17]. In this paper, we first review the epidemiology, basic characteristics, and trends of breast cancer in Korea. Then, we discuss breast cancer risk models including those that have been developed using Korean and other Asian women. Finally, we explore recent studies on personalized risk-stratified breast cancer screening and suggest ideas towards a personalized risk-stratified methodology for breast cancer screening in Korea.

BREAST CANCER EPIDEMIOLOGY, CHARACTERISTICS, AND TRENDS IN KOREA

In recent years, the incidence rate of breast cancer has increased in Korea every year, with an age-standardized rate (ASR) of 25.9/100,000 women in year 2000 and an ASR of 75.3/100,000 in 2017 [18]. According to the Korean Breast Cancer Society (KBCS) and Korea Central Cancer Registry (KCCR), the incidence of breast cancer in 2017 was highest in women 40–49 years old, with 35.9% (n=4,174) and 33.4% (n=8,867) of the diagnoses being among women in this age group, respectively. The median age at diagnosis was 51.9 years

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(KCCR data) [18]. These numbers are different from those from the U.S., where the age-standardized, delay-adjusted incidence rate for breast cancer was 126.8/100,000 women in 2012–2016 [19]. Incidence was highest among women aged 60–69 (28.2%) followed by 50–59 (23.5%), and the median age at diagnosis was 62 [20]. The 5-year survival rates in Korea for local, regional, and distant breast cancers diagnosed from 2013-2017 were 98.7%, 92.2%, and 39.9%, respectively (KCCR data) [18]. These rates are similar to those observed in the U.S., where the overall 5-year breast cancer survival rates for patients diagnosed from 2009–2015 were 98% for stage I, 92% for stage II, 75% for stage III, and 27% for stage IV [20].

The proportion of hormone receptor-positive breast cancers in Korea has increased in recent years, from 58.2% being estrogen receptor (ER)-positive in 2002 to 77.5% in 2017 and 50.7% being progesterone receptor (PR)-positive in 2002 to 66.1% in 2017. The HER2-positive rate in Korea was around 20% in 2000 and 17.8% in 2017 [21]. In comparison, based on 2012–2016 cases in the U.S., the proportion of invasive breast cancers that were hormone receptor-positive was 79%, and the proportion of HER-2 positive breast cancers was slightly lower than that of Korea, at 14% [20]. The proportion of young-onset breast cancer among newly diagnosed breast cancers, defined as invasive breast cancer in women younger than 40 years old, was 10.0 and 9.1% from KBCS data and KCCR data, respectively [18], compared to 5% of cases in the U.S. in 2012–2016 [20]. However, a recent study from a large breast cancer registry in Korea suggests that the breast cancer rate in older women is increasing at a faster rate than in younger women; thus, the proportion of young-onset breast cancers in Korea will soon approach that in Western countries [22].

BREAST CANCER RISK MODELS AND BREAST CANCER RISK PREDICTION IN KOREAN WOMEN

There are a number of risk prediction models that have been developed, each with their own strengths and limitations, and different risk models may give different scores for the same woman [23]. The following discusses the most studied breast cancer risk models and their applicability to Korean women.

A review on the quality assessment of breast cancer risk prediction models showed that four models, the Breast Cancer Risk Assessment Tool (BCRAT), the Breast Cancer Surveillance Consortium (BCSC), the Rosner and Colditz model, and the Tyrer-Cuzick (also known as the International Breast Cancer Intervention Study [IBIS]) model, were most extensively used [24]. The authors also found that the availability of breast cancer risk prediction models has increased steadily over the past three decades and that there were two new trends: the increased use of the BCSC model and the inclusion of common genetic variations in some prediction models. Below is a brief description of the four common models.

The BCRAT, also known as the modified Gail model, has been widely used and validated. The Gail model, developed in 1989, originally included five factors (age, number of first-degree relatives with breast cancer, age at birth of first child, age at menarche, and number of previous biopsies) [25]. Slight modifications were made over the years, for example, the addition of presence of atypical hyperplasia in a biopsy, and slightly different versions have been made for women of different race and ethnicities, including Asian and Pacific Islander women [26,27]. The discriminatory accuracy of BCRAT has been shown to be modest in cohort studies (area under the curves [AUCs], 0.54–0.74) in different ethnicities including

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Americans, Europeans, and Asians [28]. This model has been shown to have a discriminatory accuracy of 0.55 (95% CI, 0.50–0.59) in Korean women [29].

The BCSC model includes factors such as age, race/ethnicity, having a first-degree relative with breast cancer, history of breast biopsies, and mammographic breast density (Breast Imaging Reporting and Data System [BI-RADS]; American College of Radiology, Reston, USA). This model was developed using a cohort comprised of 3% (29,180/1,095,484) Asian or Pacific Islander women. The discriminatory accuracy of BCSC was also shown to be modest, with an AUC of 0.66 (95% CI, 0.65–0.67) [30]. A recent validation study using an independent cohort of 252,997 women in a Chicago registry demonstrated that it had an AUC of 0.63 (CI not available) and calibration expected/observed (E/O) of 0.94 (95% CI, 0.90–0.98) [31]. While this study also included approximately 3.4% Asian women, the BSCS model has not been validated in Asian women separately.

The other 2 models have also not been validated in Asian women. The Rosner and Colditz model was developed using Caucasian women. This model includes 11 risk factors: age, menarche, menopause, age at birth of first child, age at subsequent births, previous benign breast disease, hormone replacement therapy, family history, weight, body mass index, and alcohol consumption [32,33]. The discriminatory accuracy of this model has been shown to be 0.61 (95% CI, 0.58–0.64) and 0.64 (95% CI, 0.63–0.66) for ER^-/PR^- and ER^+/PR^+ tumors, respectively [33]. The Tyrer-Cuzick model was developed in the United Kingdom. This model includes genetic information (mutation of BRCA and other breast cancer susceptibility genes) and originally nine other factors, namely, age, family history, menarche, age at first birth, menopause, atypical hyperplasia, lobular carcinoma in situ, height, and body mass index (BMI) [34]. In a validation study, with the addition of mammographic density, the discriminatory accuracy of this model improved from 0.59 (95% CI, 0.56–0.61) to 0.61 (95% CI, 0.58–0.63) [35].

A recent study on the 10-year performance of breast cancer risk models found that the Tyrer-Cuzick model was well calibrated, while BCRAT underpredicted risk (ratio of expected cases to observed cases was 1.03 [95% CI, 0.96–1.12] for Tyrer-Cuzick and 0.79 [95% CI, 0.73–0.85] for BRCAT) [36]. This analysis showed that misclassification still exists, especially overprediction of risk in women in the highest quartiles and underestimation of risk in women in the lower quintiles, and highlight the need to improve power for prediction and discrimination, perhaps by incorporating mammography-based risk measures and polygenic risk score (PRS).

There has been an interest in the development and validation of a risk model reflecting Korean female breast cancer risk parameters. In 2013, a Korean Breast Cancer Risk Assessment Tool (KoBCRAT) based on data from the Seoul Breast Cancer Study (SeBCS), a case control study, and equations from the Gail model was established [37]. This model stratified the risk factors by age group. For women below age 50, a family history of breast cancer in first-degree relatives, age at menarche, menopausal status, age at first full-term pregnancy, duration of breastfeeding, oral contraceptive usage, and exercise were risk factors. On the other hand, risk factors for women aged above 50 years were a family history of breast cancer in first degree relatives, age at menarche, menopausal status/age at menopause, parity, BMI, oral contraceptive use, and exercise. The KoBCRAT was shown to have a discriminatory accuracy of 0.63 (95% CI, 0.61–0.65) in women aged < 50 years and 0.65 (95% CI, 0.61–0.68) in those aged ≥ 50 years. In the validation analyses, the AUCs of the KoBCRAT were 0.61 (95% CI, 0.49–0.72) in the Korean Multicenter Cancer Cohort (KMCC) and 0.89 for the National Cancer Center (NCC) cohort. However, this model is not yet used routinely as a clinical risk assessment tool.

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Several other countries in Asia have also developed breast cancer risk models, some of which include additional lifestyle factors and environmental exposures [38-44]. Some of the risk factors overlap between models but others do not. **Table 1** shows a brief summary of risk models developed using Asian women, including the KoBCRAT.

Table 1. Breast cancer risk models developed using Asian women

Study/Model	Year	Method	Target population	Risk factors	Discriminatory accuracy (AUC)	Calibration (E/O ratio)
Ueda et al. [38]	2003	Case-control	Japanese, 376 cases and 430 controls, any age, women from university medical center	Age of menarche, age of first birth, family history, and BMI in post-menopausal women	-	
Park et al. [37]/ KoBCRAT	2013	Case-control; validation in two independent cohorts	Korean, any age, in teaching hospitals located in urban area, 3,789 sets of cases and controls; validation in two independent cohorts (n = 11,905; n = 9,664)	Age < 50: family history, age of menarche, age of first birth, menopausal status, breast feeding duration, oral contraceptive use, exercise age ≥ 50: family history, age of menarche, menopausal status/ age of menopause, parity, BMI, oral contraceptive use, exercise	Age < 50: 0.63 (95% CI, 0.61–0.65) Age ≥ 50: 0.65 (95% CI, 0.61–0.68) Validation 1: 0.61 (95% CI, 0.49–0.72) Validation 2: 0.89 (95% CI, 0.85–0.93)	Validation 1: 0.97 (95% CI, 0.67–1.40) Validation 2: 0.96 (95% CI, 0.70–1.37)
Anothaisintawee et al. [39]	2014	Cross-sectional	Thai, any age, in university hospitals (n = 15,718)	Age, menopausal status, BMI, oral contraceptive use	0.651 (95% CI, 0.595–0.707)	1.00 (95% CI, 0.82–1.21)
Wang et al. [40]/ HRA model	2014	Case-control and cohort	Chinese, any age, 328 cases and 656 controls in case-control; validation in cohort study (n = 13,176)	Age, age of menarche, age of first birth, history of benign breast diseases, family history, history of breast feeding, history of induced abortion	0.64 (95% CI, 0.50–0.78)	-
Lee et al. [41]	2015	Case-control	Korean, any age, 4,676 cases and 4,601 controls	Age of first birth, number of children, age of menarche, BMI, family history, menopausal status, regular mammography, exercise, estrogen duration	Age < 50*: 0.6027 (95% CI, 0.6006–0.6048) to 0.6076 (95% CI, 0.6055–0.6097) Age ≥ 50†: 0.6290 (95% CI, 0.6266–0.6314) to 0.6415 (95% CI, 0.6392–0.6438)	-
Wang et al. [42]/ LASSO	2016	Case-control	Chinese, 20–84 years old, 918 cases and 923 controls	Age, number of parity, number of breast cancer cases in 1st-degree relatives, exposure to light at night, and sleep quality Premenopausal: Alcohol consumption Postmenopausal: BMI, age of menarche, age of first birth, breast feeding, oral contraceptive usage, hormone replacement treatment, and history of benign breast diseases	Premenopausal: 0.640 (95% CI, 0.598–0.681) Postmenopausal: 0.655 (95% CI, 0.621–0.653)	-
Zhao et al. [43]	2017	Cohort	Chinese, age 45–70 years (n = 3,030)	HRA model [40]	0.73 (95% CI, 0.64–0.83)	-
Wang et al. [44]/ Han Chinese Breast Cancer Prediction model	2019	Case-control and cohort	Chinese, 328 cases and 656 controls in case-control; validation in cohort study (13,176 women)	Number of abortions, age of first birth, history of benign breast disease, BMI, family history, and life satisfaction scores	Validation: 0.64 (95% CI, 0.55–0.72)	Validation: 1.03 (95% CI, 0.74–1.49)

Fields marked with a dash indicate data not available.
AUC = area under the curve; E/O = expected/observed; KoBCRAT = Korean Breast Cancer Risk Assessment Tool; BMI = body mass index; CI = confidence interval; HRA = health risk appraisal; LASSO = least absolute shrinkage and selection operator; SVM = support vector machine; ANN = artificial neural network; BN = Bayesian network.
Three computational methods were used: *Age > 50: SVM, 0.6076 (95% CI, 0.6055–0.6097); ANN, 0.6060 (95% CI, 0.6040–0.6080); and BN, 0.6027 (95% CI 0.6006–0.6048); †Age ≥ 50: SVM, 0.6415 (95% CI, 0.6392–0.6438); ANN, 0.6383 (95% CI, 0.6359–0.6407); and BN, 0.6290 (95% CI, 0.6266–0.6314).

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Due to limited breast screening availability and breast biopsies in some regions of Asia [44], the number of previous biopsies was not included in many risk models developed using Asian women. However, Asian risk models included various different factors, including exposure to light at night, sleep quality, and life satisfaction score. Although these risk models were developed and tested in Asian women, they have not been validated in separate populations, and different models may still yield different risk scores for the same woman. In order to accurately identify high-risk women for risk-based screening in Korean women, further study is needed.

TOWARD PERSONALIZED BREAST CANCER SCREENING IN KOREA: INCORPORATING PRS INTO RISK ASSESSMENT

For personalized cancer screening, accurate estimation of an individual's susceptibility to cancer is of utmost importance. Like other cancers, breast cancer has multi-factorial etiologies including a genetic component. In addition to genetic mutations, genome-wide association studies (GWAS) have enabled the identification of numerous genetic variations, or single nucleotide polymorphisms (SNPs), that are associated with complex human traits and disease, including cancer, obesity, cardiovascular disease, and Alzheimer's disease [45]. While each SNP does not have a large effect size, the combinations of SNPs often do [46,47]. As described, there has been an effort to have more predictive value for risk classification with PRS added to various models.

For example, a study on 981 multi-ethnic women from San Francisco Mammography Registry (SFMR) showed that addition of a PRS comprised of 83 SNPs to the BCSC model modestly improved its AUC from 0.62 (95% CI, 0.59–0.66) to 0.65 (95% CI, 0.61–0.68) [48]. Addition of a PRS to the Gail and Tyrer-Cuzick models also showed modest improvements in various other studies, up to 0.06, depending on the risk model and study population [49-51]. The BCRAT and Rosner-Colditz models were also recently tested by Zhang et al. [52] by adding PRS and other factors such as mammographic density and endogenous hormones. Overall, the AUC for the BCRAT model improved from 0.56 (95% CI, 0.54–0.58) to 0.65 (95% CI, 0.64–0.66), and the AUC for the Rosner-Colditz model improved from 0.61 (95% CI, 0.59–0.63) to 0.68 (95% CI, 0.67–0.69). As expected, the addition of other factors beyond PRS improved the AUCs. Interestingly, the AUCs were slightly different for women in different subgroups, for example, premenopausal women compared to postmenopausal women who were using versus not using hormone therapy [52].

While these findings support the potential clinical utility of incorporating PRS into existing breast cancer risk models as a screening tool, the SNPs that comprise the PRS should be applicable to the population being screened. To this end, some SNPs associated with breast cancer risk have been identified in race/ethnicity-specific cohorts [53-56]. In addition, new risk variants in genes such as *BRCA1*, *BRCA2*, *CHEK2*, and *PALB2,* were detected in a study cohort of East Asian women, including 2,291 Korean women in the Breast Cancer Association Consortium (BCAC), compared to European ancestry [57]. Notably, a PRS comprised of 44 SNPs had an AUC of 0.61 (95% CI not available) in East Asian women in the BCAC which, as noted in the previous study, included 2,291 Korean women [56]. In Korean women specifically, the lifetime risk (age 20–80) of developing breast cancer by age 80 for the lowest 1% of the PRS was 1.31%, whereas the estimated risk for the highest 1% of the PRS was 9.81% for Korean women [56]. These findings suggest that PRS can be a valuable tool for risk stratification in Korean women.

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Table 2. Studies on breast cancer risk models incorporating PRS in Asia

Study	Year	Method	Target population	Risk factors	Discriminatory accuracy (AUC)
Lee et al. [58]	2014	Case-control	Singapore Chinese, age 45–74 years, 1,212 controls and 411 cases	vGail* (age at menarche, age at first live birth, number of 1st degree relatives with breast cancer), BMI, PRS (51 SNPs)	-†
Lee et al. [59]	2015	Prospective cohort, 17 years follow-up	Singapore, age 50–64 years, 24,161 women	vGail (age at menarche, age at first live birth, number of 1st degree relatives with breast cancer), BMI, mean breast dense area, PRS (75 SNPs)	vGail + BMI: 0.62 (95% CI, 0.60–0.64) vGail + BMI + Density: 0.65 (95% CI, 0.63–0.66) vGail + BMI + Density + GRS: 0.66 (95% CI, 0.65–0.68)
Wen et al. [56]	2016	Case-control	East Asians participating in nine studies in the BCAC that were conducted in China, Japan, South Korea, Thailand, and Malaysia, any age, 11,612 controls and 11,760 cases	44 SNPs	0.606 (SD, 0.38)
Hsieh et al. [60]	2017	Case-control	Taiwanese, age 20–90 years in 4 hospitals, 514 controls and 446 cases	Age, BMI, age at menarche, parity, menopausal status, PRS (6 SNPs)	Without PRS: 0.63 With PRS: 0.67 PRS only: 0.60
Chan et al. [61]	2018	Case-control	Singapore Chinese, any age, 243 controls and 301 cases	PRS model 1: 46 SNPs PRS model 2: 11 SNPs PRS model 3: 9 SNPs	0.566 (95% CI, 0.517–0.614) 0.565 (95% CI, 0.516–0.613) 0.557 (95% CI, 0.508–0.606)

PRS = polygenic risk scores; AUC = area under the curve; BMI = body mass index; SNP = single nucleotide polymorphism; CI = confidence interval; BCAC = Breast Cancer Association Consortium; SD = standard deviation.
*Variables of Gail model; †This study showed that addition of a Genetic Risk Score with risk factors reclassified 6.2% women for their absolute risk of breast cancer in the next 5 years.

In addition, there are some studies that showed that PRS can improve the discrimination in Asian women above existing risk models [56,58-61]. For example, Shieh et al. showed that a PRS comprised of 76 SNPs improved the AUC of the BCSC model in East Asian women in San Francisco, California from 0.62 (95% CI, 0.59–0.66) to 0.72 (95% CI, 0.62–0.82) [48]. Furthermore, addition of a PRS using 6 SNPs to a risk model containing clinical risk factors, such as BMI, waist-to-hip ratio, parity number, and menopause status, was shown to improve the AUC from 0.63 to 0.67 (95% CI not available) in a cohort of Taiwanese women (**Table 2**) [60]. **Table 2** shows the comparison of studies on PRS for breast cancer risk prediction in Asia.

While there were only two studies examining the effect of adding PRS to breast cancer risk models among women in Asia, they both showed small improvements in AUC (0.01 in the study by Lee et al. [59] and 0.04 in the study by Hsieh et al. [60]). These small improvements are generally consistent with the improvements seen in many Western studies [48-51] but slightly lower than the 0.10 increase in AUC observed among Asian women in the Shieh et al.'s study [48]. Differences in improvements in AUC may be attributable to the number of SNPs in the PRS, the effect size of each individual SNP, and the presence or absence of specific factors in the original risk model. It is also possible that addition of PRS may improve AUC more in specific subsets of the study populations, for example, by menopause or hormone therapy status, as was seen in the study by Zhang et al. [52]. Thus, it is difficult to predict how much improvement, if any, a PRS will make upon the performance of a given risk model; this needs to be tested. It is also important to consider that even small increases in AUC can lead to several percent of the population being reclassified into different risk categories, thereby warranting a change in their clinical management [62]. Thus, any improvement in the predictive accuracy of a risk model would have clinical utility for breast cancer early prevention and risk-based screening. A UK cost-effectiveness study which used a life-table model of a hypothetical cohort of 364,500 women showed that risk-stratified screening for breast cancer is associated with reduced overdiagnosis and reduced cost of screening while maintaining quality-adjusted life-years gained and reduced breast cancer deaths [63]. As part of the effort to improve cancer control and prevention in Korea, the

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development of personalized cancer screening has been suggested, consistent with the worldwide trend [64]. However, it is essential to assess a model's predictive performance in an external cohort from the one used for developing the model. In addition to the clinical validity of the integrative prediction model, aspects to be considered in developing a personalized breast cancer screening program include patients' willingness to undergo breast cancer risk assessment. To this end, several studies, such as the PROCAS study in the UK [65], the KARMA study in Sweden [66], and the Athena Breast Health Network in the U.S. [67], have shown the feasibility of conducting risk assessment in the context of clinical breast mammography screening. Also, in the absence of results from appropriate randomized trials, no firm evidence exists to support risk-based breast cancer screening in the general population. In this aspect, the Women Informed to Screen Depending On Measures of risk (WISDOM) study, being conducted in the U.S., is unique in that it is a clinical trial testing the safety, efficacy, and acceptability of risk-based (using the BCSC model with PRS) breast cancer screening compared to annual screening [15]. Trials like this will hopefully end the long-standing debate of how often a woman should undergo mammography and at what age she should start.

Based on the available literature, we suggest that more studies are needed to identify and validate SNPs for breast cancer susceptibility in Korean women such as the 44 SNPs identified in the study by Wen et al. [56] and to incorporate these into well characterized models such as KoBCRAT [37] to investigate the clinical utility of PRS with traditional breast cancer risk models most applicable to Korean women. Well-designed, randomized, and controlled clinical trials would demonstrate if a risk-stratified screening strategy would have clinical utility for Korean women. We can refer to the methodology of the WISDOM Study for a reference tolerant and adaptive design that encourages women to be randomized but also allows self-assignment for those with strong personal preference for either annual or risk-based screening [15].

While personalized risk assessment and screening hold promise for improving breast cancer screening in the population, remaining issues include the still-limited discriminatory power of current breast cancer risk models, even with the addition of PRS [68]. In addition, implementation barriers include those that may be present at the organizational level, low clinician and patient knowledge, and ethical or social issues [69]. For personalized risk assessment and screening to succeed, the engagement of policy makers, guideline organizations that include multiple medical specialties, and the patient community is essential, and consensus should be reached to define acceptable parameters of risk assessment, stratification and screening recommendations. Further work is needed to address these challenges.

CONCLUSIONS

While strategies such as the national screening program and activities put forth by non-governmental organizations such as the KBCS have contributed to increasing breast cancer awareness and screening, there is a need to step forward to improve the effectiveness and efficiency of breast cancer screening amidst the continuously increasing incidence rate of breast cancer in Korea. While some challenges remain, a risk-based screening approach should be seriously considered for development and implementation in Korea in the current era of personalized medicine.

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