Journal of Breast Cancer

J Breast Cancer 2011 June; 14(2): 79-87 DOI: 10.4048/jbc.2011.14.2.79

REVIEW ARTICLE

Risk Factors and Control Strategies for the Rapidly Rising Rate of Breast Cancer in Korea

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Due to the aging population and tremendous changes in life style over the past decades, cancer has been the leading cause of death in Korea. The incidence rate of breast cancer is the second highest in Korea, and it has shown an annual increase of 6.8% for the past 6 years. The major risk factors of breast cancer in Korean women are as follows: Early menarche, late menopause, late full-term pregnancy (FTP), and low numbers of FTP. Height and body mass index increased the risk of breast cancer in postmenopausal women only. There are ethnic variations in breast cancer due to the differences in genetic susceptibility or exposure to etiologic agent. With the epidemiological evidences on the possibility of further increase of breast cancer in Korea, the Korean Government began implementing the National Cancer Screening Program against breast cancer in 2002. Five-year survival rates for female breast cancer have improved significantly from 78.0% in early 1993-1995 to 90.0% in 2004-2008. This data indicate that improvement of the survival rate may be partially due to the early diagnosis of breast cancer as well as the increased public awareness about the significance of early detection and organized cancer screening program. The current primary prevention programs are geared towards strengthening national prevention campaigns. In accordance with the improvement in 5-year survival rate, the overall cancer mortality has started to decrease. However, breast cancer death rate and incidence rates are still increasing, which need further organized effort by the Korean Government.

Key Words: *Breast neoplasms, Korea, Risk factors*

INTRODUCTION

Cancer has been the leading cause of death in Korea since 1983 due to the aging population and tremendous changes in lifestyle, and one out six Koreans died of cancer that year. The proportion of cancer deaths has increased every year since then, accounting for 33.4% of all deaths in 2009 [1]. This means that more than one of every four Koreans is a victim of cancer. Increases in life expectancy also cause increase in cancer incidence. One of three men who lives to the age of 77 may develop cancer, and three of ten women who lives to age 83 may develop cancer. During the first term of the 10-year plan of National Cancer Control since 1995, a significant reduction in cancer mortality rates for stomach and liver cancer was observed in men, and cervical cancer in women in Korea. However, mortalities from lung and colon cancer in men and breast cancer in women have increased. Lung cancer mortality decreased in men during the latter period of the first term [2]. The most dramatic change has comes from breast cancer. The percent increase in breast cancer mortality for middle-aged women from the mid-1980s to the mid-1990s was the highest in Korea, followed by China, and Japan [3-5].

In particular, the incidence of breast cancer, which was previously the second leading cause of cancer in Korea, has increased 6.8% annually during the last 6 years. This is a unique epidemiological feature that has been observed in Asia over the past few decades. Among men, stomach cancer has the highest occurrence, followed by lung, liver, colorectal, and prostate. In women, the two most common cancers are breast and thyroid, followed by stomach, colorectal, lung, and cervical [2,6].

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The present research has been supported by Korea Breast Cancer Foundation.

Received: May 4, 2011 **Accepted:** June 3, 2011

RISK FACTORS OF BREAST CANCER

Risk factors for breast cancer identified in Korea

Beginning in the early 1990s, two large-scale multi-center

http://ejbc.kr | pISSN 1738-6756
eISSN 2092-9900

case-control studies were conducted to identify breast cancer risk factors in Korea. A fundamental question was whether there were differences in established risk and protective factors between Western and Korean women. As a result, the main breast cancer risk factors in Korean women early age at menarche, which was rather weak but significant, and late age at menopause. Late age at first full-term pregnancy (FTP) and a smaller number of FTPs clearly showed an increased risk for breast cancer, probably due to changes in breast tissue susceptibility or to hormonal milieu [7,8]. A dose-dependent increasing trend for breast cancer risk occurs as a result of life-time exposure to estrogen, which is roughly defined by the interval between menarche and menopause. Breast feeding has been a controversial subject among breast cancer epidemiologists. A longer duration of breast feeding per child has a protective effect against breast cancer, independent of parity. This is particularly evident when the analysis is restricted to the first child [9]. Similar findings have been published in Japan [10,11].

Height is also a risk factor for breast cancer but is significant only for postmenopausal women, which might be related to growth factors. Similarly, obesity, indicated by body mass index, increases the risk of breast cancer in postmenopausal women [12,13]. This is a very similar to findings observed in the U.S. and Japan [14], which is highly relevant to the estrogen-augmented-by-progesterone hypothesis [15]. Despite the possibility of recall bias in this case-control study, late teen body weight showed a statistically significant association with breast cancer risk only in postmenopausal women, which supports nutritional status adolescents [9].

Most of the established risk and protective factors observed in Western countries are similarly observed in Korean women. However, risk factors such as smoking, physical inactivity, nonsteroidal anti-inflammatory drug and oral contraceptives use, as well as exposure to ionizing radiation need to be further evaluated. Evidence suggests that most of the risk factors are closely related with estrogen and progesterone levels, which have been hypothesized to be causative agents in breast cancer etiology. Among the risk factors identified in a Korean study, the protective effect of breast feeding against breast cancer is generally more prominent in Asian countries, whereas early menarche and hormone replacement therapy show a very weak association, and postmenopausal obesity shows a moderate association.

Reasons for international variations in breast cancer incidence

The next question is why is there such a wide variation in cancer incidence throughout the world, even though many common risk factors for breast cancer are shared among different countries. Apparently the incidence is highest in North America, Western Europe, and Australia, whereas it is relatively low in Japan and Korea.

One of the reasons is that the magnitude of exposure to etiological agents may be different by ethnicity and country. Serum levels of 17β-estradiol (E2) among Korean women are much lower than those of Western women [16] and even lower than those of Japanese women [17]. Differences in the relative exposure to risk factors may be an explanation for the ethnic differences in breast cancer incidence.

One of the explanations of why Koreans have been maintaining such a lower incidence compared to Western women may be differences in hormone receptor status. It is well-known that receptor positivity is essential for breast cancer development, and the age-incidence curve is dependent on how many cases have the receptor in the population [18]. Estrogen receptor (ER) or progesterone (PG) receptor (PR) positivity is about 65.9% among breast cancer cases, whereas a lower frequency of ER/PR expression occurs in Korean women.

Age incidence curve of breast cancer

Recent statistics on age-specific female breast cancer rates among Korean females appear to be somewhat different figures stomach, lung, and colorectal cancers rates, showing their highest peak in the 45-49 years age group. A similar finding has also been observed for thyroid cancer. Although the breast cancer incidence has more than doubled in the last decade, the peak age group has not changed [19]. The age incidence curve of breast cancer is partly influenced by hormones receptor status of the Korean female population. However, it must be emphasized that there is a strong generational cohort effect in terms of breast cancer occurrence in Korean women. It has been demonstrated that the number of people in their late 60-70s was 1.2 to 2.1 times higher in 2003 than it was in 1984. These data are based on the age-cohort effect model [20].

Another reason may be due to the marked increase in breast cancer screening experience particularly in middle-aged Korean women, i.e., higher rate of screening rates among women aged in their 40s and 50s, which is compatible with the age-incidence curve findings [19]. Particularly, in large metropolitan areas including Seoul, more educated and more prosperous women tend to visit private breast clinics more frequently to undergo breast cancer examinations at their own expense or using private health insurance. This would be one reason why the incidence of breast cancer is high in middle-aged women in Korea.

Based on this evidences, it can be speculated that, when the occurrence of breast cancer increases to 80 or more than 100 per 100,000 persons in the future in Korea, it will influence the increase in serum E2/PG level, the most significant risk

 DOI: 10.4048/jbc.2011.14.2.79

factor. Furthermore, the proportion of women with positive ER/PR will reach more than 80%, and ultimately the age curve will be changed to that of the current curve observed in Western women.

GENETIC POLYMORPHISMS OF BREAST CANCER

Differences in genetic susceptibility to breast cancer

Human genetic variations are involved associated with disease susceptibility. Different from the concepts of gene variation in biomarkers, genetic variations in human genome epidemiology determine an individual's disease predisposition and progression and detect individual susceptibility to diseases during all periods from preclinical steps to death.

The first molecular epidemiological study from our group was published in 2000 and deletion polymorphisms in the GSTM1 and GSTT1 genes were identified as breast cancer risk factors [21]. Inherited differences in activation or deactivation of environmental carcinogens, such as by glutathione-S-transferases coded by GSTM1 and GSTT1 modify individual susceptibility to breast cancer development. Moreover, individuals with the Val allele of GSTP1 Ile105Val have a 0.3-fold reduced risk for breast cancer [22]. Both the GSTM1 and GSTT1 genetic polymorphisms have gene-gene interaction effects with NAT1 or two polymorphisms to modify breast cancer risk, although NAT 1 and 2 have no significant independent effect on breast cancer risk [23]. The Gln containing homogenotype of the XRCC1 codon 399 polymorphism is associated with a 3.8-fold higher risk for premenopausal breast cancer [24].

Not only xenobiotic metabolic polymorphisms of xenobiotic metabolism but those of estrogen metabolism are involved in breast cancer risk. Breast cancer risk decreases 0.4-fold in women with the XbaI X allele containing genotypes [25]. The catechol O-methyl transferase (COMT) Val158Met gene, which codes key enzymes involved in converting catechol-estrogens to methoxy-estrogens, reveals a 1.7-fold increased risk for breast cancer [26]. The glutathione S-transferase (GST) polymorphisms for xenobiotic metabolism and the COMT polymorphism for estrogen metabolism have a combined effect, which increases breast cancer risk [27]. The cytochrome P450 1A1 (CYP1A1) genes, which codes a key enzyme involved in converting estrone/E2 to catechol-estrogens such as 2-hydroxyestradiol shows a 0.3-fold decreased risk for breast cancer compared to CA/CA diplotypes of CYP1A1 MspI (rs4646903) and Ile462Val polymorphisms (rs1048943) [28]. The CYP17 gene, which codes a key enzymes involved in the conversion of 17-hydroxypregnenolone to 17-hydroxyprogesterone or dehyroepiandrosterone to androstenedione during estrogen synthesis, has no independent role in breast cancer development [29]. The SULT1A1 and E1 genes coding human sulfotransferases are involved in converting estrogen to E2. The CTA-CCA haplotype of SULT1E1 (c.779G > A, *14A > G, and *85C > T) shows a 0.5-fold reduced risk of breast cancer, whereas no significant association with the SULT1A1 genes was found in our study [30]. A number of DNA repair, genes associated with cytokines, and cell cycle control are related to breast cancer risk. Women with a decrease in the ATM ATTGT haplotype, composed of 5144A > T, IVS21 +1049T > C, IVS33-55T > C, IVS34+60G > A, and 3393T > G have an, increased breast cancer risk [31]. The T allele containing the RAD52 2259, -93 GG genotype of hMLH1 and the T allele containing the ERCC1 8092 genotype are associated with a 1.3-1.7-fold increased breast cancer and these of RAD 52 and ERCC1 354 genotypes are more evident in ER/PR negative cases by up to 2.0 fold [32]. X-ray cross-complementing group 3 (XRCC3) is protein components involved in the homologous recombination repair pathway that repairs radiation-induced DNA damage. Our study showed no association with breast cancer risk; however, a meta-analysis including our results suggested that the Met allele containing the XRCC3 Thr241Met genotypes weakly increases breast cancer risk compared to the Thr/Thr genotype [33]. Other genes involved in the DNA repair system, such as hOGG1 Ser326Cys, XRCC4 c. 921G > T, RAD51 nt 135G > C and nt 172G > T, LIG1exon 6 nt 551A > C, ERCC1 3VUTRc. 8092C > A, and hMLH1 5Vexon8 Ile219Val (A > G), are unlikely to play a modifying role in individual susceptibility to breast cancer among Korean women [34]. Cyclin D1 (CCND1) and CDK-activating kinase 7 (CDK7) genes code key regulators of cell cycle progression and cell development. Women carrying the CDK7 TT genotype have a weakly increased risk of breast cancer (1.4 fold), whereas no significant association with the CCND1 genetic polymorphism was found [36]. CDK7 has a weak gene-gene interaction with ESR1 P325P; the combination those with the CDK7 TT and ESR1 P325P combination CC had a 1.7-fold increased risk for breast cancer [35].

Innate immune and inflammatory responses may be related to breast cancer development. Endogenous cytokine families involved in inflammatory and immunological responses include interleukin (IL)-1, IL-1α, IL-1β and an IL-1 receptor antagonist encoded by IL-1RN. The two-alleles of IL-1RN 86-bp VNTR are associated with a decreased breast cancer risk with marginal significance, whereas the C containing genotypes of the IL-1βB -31C/T polymorphism have no independent role in a decreased risk for breast cancer. However the combination of both the IL-1β C-allele and IL-1RN two-allele containing genotypes have a gene-gene interaction that significantly decreases the risk of breast cancer by 0.6-fold [36]. Tumor necrosis factor beta (TNF-β) is a pro-inflammatory cytokine secreted by lymphocytes and has both anti-tumor and pro-cancer activity and Transforming growth factor beta (TGF-β) acts as a potent inhibitor of proliferation of epithelial, endothelial and hematopoietic cells. Individuals, particularly postmenopausal women, with C and G containing genotypes of TGF-β1 T29C and TNF-β A252G are at a 1.3- and 1.7-fold increased risk for breast cancer, respectively [37].

Apoptosis is important in cancer development and hypoxia inducible factor 1 (HIF-1) and caspase-8 (CASP8) mediate a broad cellular response, which leads to tumorigenesis and tumor aggressiveness. The Ser allele contained in the HIF-1A P582S genotypes and the T allele contained in the CASP8 genotypes are weakly involved in breast cancer susceptibility (1.1 fold). These associations are particularly prominent in aggressive tumors such as larger tumor 2 cm (10 fold) with HIF-1A genes and in ER or PR negative cases (1.3 fold) with the CASP8 gene, respectively [38,39].

We screened candidate genetic variants in an affordable, high-throughput manner using two kinds of Illumina GoldenGate. These genes are involved in the pathways controlling the innate immune and inflammatory responses, cytokines, apoptosis/anti-apoptosis, and DNA repair. Seventeen genes related to innate immunity on the first 1,536 single-nucleotide polymorphism (SNP) panel such as OR10J3, FCER1A,NCF4, CNTNAP1, CTNNB1, KLKB1, ITGB2, ALOX12B, KLK2, IRAK3, KLK4, STAT6, NCF2, CCL1, C1QR1, MBP, and NOS1, were associated with breast cancer risk in single SNP analyses. Of them, OR10J3 (rs2494251) and FCER1A (rs7548864) were selected as significant candidate genes related to breast cancer risk in Korean women ($p = 1.2 \times 10^{-4}$ and 7.7×10^{-4}, respectively) [40]. Five genes on the second 1,536 SNP panel such as IL1A, TNFRSF10B, TNFRSF1B, ICAM, and TNFSF9 were primarily screened. Of them, a common genetic variant in IL1A was strongly associated with breast cancer risk ($p = 6 \times 10^{-7}$). We have performed a large-scale genome-wide association studies for breast cancer risk to find susceptible genetic factors among Korean women and those findings will be published shortly.

Gene-environment interaction

GST genetic variations are related to alcohol consumption, and modify breast cancer risk up to 7-fold [21]. A significant interaction was observed between the GSTP1 genotype and alcohol consumption (p for interaction = 0.01), compared with never-drinking women with the Ile/Ile genotype. Ever-drinking women with the GSTP1 Val allele had almost a 3-fold increased risk of for breast cancer, whereas never-drinking women with the Val allele had a 0.5-fold reduced risk. A similar interaction with alcohol consumption was reported in cysteine-containing allele positive genotypes of CYP2E1 in the 5′ flanking region (RsaI) and the interaction increased breast cancer risk up to 3-fold. In contrast, no significant interaction was observed between the ALDH2 Glu487Lys polymorphism and alcohol consumption in Korean women [41].

GSTs gene variations interacted with reproductive factors such as a high risk group for parity (age at first full-term pregnancy ≥ 30 years and nulliparous women) to increase the breast cancer risk up to 88-fold [42]. A combined effect on breast cancer risk was also observed between body mass index (BMI); women with a higher BMI and the IL-1RN non-2 allele had a 1.7-fold higher risk than women with a lower BMI and the IL-1RN*2 genotypes [36]. CYP17 and TGF-β1 genes also show a gene-environment interaction with BMI. Heavier women (BMI > 22 kg/m^2 or median level BMI > 22.8 kg/m^2) with the CYP17 A1 and TGF-b1 c allele containing genotypes have a 2-fold increased risk for breast cancer [29,37]. The interaction effect between the CA/CA diplotypes in CYP1A1 MspI, Ile462Val polymorphisms, and BMI also had a more pronounced effect than the CYP1A1 gene effect. Women with a lower BMI have a 0.2-fold decreased risk for breast cancer. The CYP1A1 diplotypes had another gene-environment interaction with lifetime estrogen exposure. Women with a shorter lifetime estrogen exposure have a 0.2-fold significantly reduced risk for breast cancer [28].

Breast cancer survivals

Estrogen is conjugated by sulfotransferases, and SULT1E1 has the highest affinity for estrogens. A SULT1E1 polymorphism related to better breast cancer survival, particularly among women with ER negative breast cancer [30].

A summary of our international collaboration on a case-control study for genetic polymorphism of breast cancer shows relatively weak power in terms of sample size of a Korean study showed very good results on breast cancer [43].

Although data on the influence of inherited factors to breast cancer is limited, differences in genetic constitution by different ethnic groups may be a clue to explain racial differences. The KOJACH study is an example of an international collaborative study on colorectal and breast cancer that included three geographically and historically close countries, Japan, Korea, and China, but they have preserved their own cultures for a long time. This study will provide additional supportive results of protective and risk factors with increased power due to data pooling.

Future trends in breast cancer in Korea

According to statistical projections, the Korean population is expected to become an aged society in the near future. Many

DOI: 10.4048/jbc.2011.14.2.79

countries in Asia including Korea are now experiencing low fertility and an aged society, so we expect that more cancer cases will occur in Korea in the near future.

Korea has been experiencing a considerable change in lifestyle pattern including changes in eating habits. For example, grain intake has been declining continuously, whereas meat consumption has risen steadily over the last four decades. Additionally, dramatic changes in reproductive behaviors, including age at first marriage, fertility, and age at menarche may have the greatest contribution [44]. If the current trend continues, we can expect breast cancer incidence to rise gradually in the future. Currently, more and more mothers are resorting to formula feeding in Korea. This phenomenon is probably due to the increasing role of working women in a changing social environment such as difficulty feeding their babies during working hours. However, special attention should be given to promote breast feeding by organizing public campaigns.

Age-adjusted breast cancer incidence rates among Asian migrants living in Los Angeles suggest lifestyle factors including diet may play a role in breast cancer etiology. Korean migrants showed the lowest rate of breast cancer compared to Japanese, Chinese, and even Filipinos, probably due to the relatively short history of immigration to the U.S. [45]. However, when compared to the incidence among Koreans living in Korea, Korean migrants have substantially higher incidence levels of breast cancer than women in their mother country, which suggests that breast cancer might further be increased based on changes in environmental habits including diet. Numerous epidemiological studies have been conducted on the possibility of a further increase in breast cancer in Korea. Based on mortality trends over the last two decades, breast cancer mortality in Korea is estimated to increase almost four times by 2020 compared to 1983 [20].

CONTROL STRATEGY OF BREAST CANCER

Control strategy against the breast cancer burden in Korea

Disease burden is composed of the burden due to premature death and disability, and cancer imposes a considerable burden on the nation's economy. The estimated total cost caused by cancer in 2005 is an estimated 14 billion USD, which is 1.7% of the national GDP, and 0.7 billion USD is the estimated cost for breast cancer alone (0.1% of GDP). Thus, reducing cancer burden by promoting national cancer control activities becomes one of the most urgent health issues in Korea [3-5].

World Health Organization (WHO) declared in 2002 that one third of all human cancers can be prevented by stopping-smoking, receiving vaccinations, and diet control. Another one third can be cured through early detection such as screening, and the remaining one third will require palliative medicine to ensure quality of life. At the General Assembly in May 2005, 192 WHO member states accepted a resolution for "Cancer Prevention and Control," which prioritized cancer control for the first time.

The Korean government began implementing the National Cancer Screening Program (NCSP) in 1999 and has expanded its target population and target cancers since then. Currently, the NCSP provides free screening for (stomach, breast, cervical, liver, and colorectal cancers) to Medical Aid and National Health Insurance Corporation (NHIC) beneficiaries within the lower 50% contribution which covers about 56% of the entire population. By initiating the NCSP in 1999, the Korean government has expanded its target population and target cancers. Currently, the NCSP provides both Medical Aids beneficiaries and low-income NHIC beneficiaries with free-of-charge screening services for stomach, breast, cervical, liver, and colorectal cancers [46].

Korea has a system of universal coverage of medical health care through National Health Insurance [47]. The eligible population that requires screening includes women ≥30 years old and men over ≥40 years old, and the target population was about 13 million in 2009 [48]. Most of these patients are NHIC beneficiaries, and about 4% are Medical Aid recipients. The actual number of patients covered by the NSCP was 7.3 million (coverage rate, 56.2%) in 2009 [48,49]. These patients receive free screening services for five major types of cancer by the guidelines. The Ministry of Health and Welfare, in collaboration with related academic societies, has developed national protocol guidelines for organized cancer screening in Korea. Breast cancer screening was introduced at the start of the NCSP, and women aged 40 or older are recommended to undergo a mammogram every 2 years.

Screening rates based on the NCSP information system were 12.7% in 2002, and improved gradually to 32.7% in 2009. The nationwide survey for health screening performance rate showed that the screening rates for stomach, colorectal, liver, breast, and cervical cancers were 38.8% in 2004 and 56.6% in 2010 when the NCSP and the screening program were supported by National Health Insurance in Korea. Among people who had screening performed for five cancer types, 67.8% used the organized cancer screening program in 2010. The nationwide survey also revealed that the life-time screening rates for individuals, who had taken at least one cancer screening in the given year under the screening guidelines recommended by the National Cancer Center and the Ministry of Health and Welfare was 72.1% in 2009 [49].

Survival rate is a key barometer indicating the effectiveness of the NCSP. Although overall cancer mortality has not been reduced significantly, the 5-year survival rate is beginning to improve. As announced by the Korea Central Cancer Registry, we have a very high 5-year survival rate for cancers of the thyroid, breast, and cervix of more than 80%. Five-year survival rates for female breast cancer have improved during the last 15 years from 78.0% in 1993-1995 to 90.0% in 2004-2008 [2]. These data indicate that the improvement in survival rate may be partly due to early diagnosis at an earlier breast cancer stage.

The most noteworthy figure is the higher survival rate of stomach and liver cancer in Korea and Japan than that in the U.S.. The survival rates for colorectal and breast cancer are very similar among Korea, Japan, and the U.S. private clinics participate in breast cancer screening including privately-insured patients. The participation rate in breast cancer screening is contributed both by the national screening program and private screening. The average rate of participation in public and private cancer screening programs including the NCSP 61.1% for breast cancer and 62.9% for cervical cancer in 2010 [49]. The participation rate in NCSP breast screening has also increased from 18.2% in 2004 to 35.0% in 2008 [50]. Although the participation rate for NCSP breast cancer screening is increasing for all target populations that of the Medical Aids recipients is in a steady state compared to that in NHIC beneficiaries [51]. Compared to the cancer screening participation rate in the U.S., which is 66.9% for breast and 77.9% for cervical cancer screening, Korea's rate still remains relatively low. This is partly influenced by advertisements about the significance of early cancer detection and the organized cancer screening program.

To address cancer at the national level, the Korean government developed a 10-year plan for cancer control in 1996. As part of the plan, the NCSP was introduced in 1999, and in 2001, the National Cancer Center headquarters became involved in the fight against cancer.

The legal framework for controlling cancer was later established in 2003 when the National Cancer Control Law was legislated. Nine regional cancer centers were designated in 2004, and in 2006, the second term 10-year plan for cancer control was initiated [52].

National action for primary prevention

The second-term plan aims to reduce the cancer burden significantly through primary, secondary, and tertiary preventive efforts. The primary prevention programs currently underway are for strengthening national prevention campaigns such as smoking cessation and dissemination of cancer prevention guidelines. Providing the target population with mass-screening service, strengthening financial support and improving quality of life through quality care for cancer patients are some of the government's secondary and tertiary programs. The government is also strengthening its capacity for cancer control through a sophisticated nationwide cancer registry program, investing more in research and development activities, enhancing public awareness about all aspects of cancer, and nurturing next-generation cancer specialists.

In 2007, the government developed ten codes of conduct for cancer prevention to help the general public lead a cancer-free life by following prevention guidelines. The codes of conducts include quitting smoking, eating sufficient fruits and vegetables, reducing salt intake, not drinking alcohol excessively, exercising regularly, maintaining a healthy body weight, receiving a hepatitis B vaccine, maintaining safe sexual behavior, and avoiding occupational cancer risks. Various leaflets and posters encourage public awareness for cancer prevention.

The National Cancer Information Center was opened in 2005. The web portal services includes information on the various characteristics of all types of cancers, FAQs, national cancer statistics, a large selection of educational materials, and a medical vocabulary services. The center also provides the public with counseling at a toll-free phone number. To increase public awareness about the importance of cancer prevention activities, the National Cancer Control Act designated March 21 as cancer prevention day. The first anniversary was celebrated and included many events to increase knowledge about cancer prevention activities.

The Center for Cancer Prevention and Early Detection was opened at the National Cancer Center, Korea in June 2007 to provide and develop effective early screening tests in Korea. A customized cancer prevention service is provided at this facility. Many invited guests from the government, national assembly, businessmen, foreign ambassadors, professors, scientists, and outstanding international figures from the Nation Cancer Center, Japan, International Agency for Research on Cancer, and the National Cancer Institute, U.S. came to celebrate this facility on June 18 and 19, 2007. The President of the Republic of Korea delivered a special message on "Cancer is preventable, and further strengthening of early detection is needed to conquer the cancer. We call that day the beginning of the era of cancer prevention."

Voluntary movement by non-governmental organizations

To increase public awareness about the importance of cancer prevention, various types of exhibitions and campaigns have been designed and conducted by non-governmental organizations, including the Korean Breast Cancer Society and Korean Breast Foundation. Founded in 2000 as a non-profit organization, the Korean Breast Foundation aims to improve the quality of life for women through public awareness, various cam-

 DOI: 10.4048/jbc.2011.14.2.79

paigns, medical aids for patients with poor economic status, and web-based medical consultations. During the Pink Ribbon campaign in several major cities each year, free mammography examinations were provided irregularly but continuously. The Pink Illumination Exhibition, organized by Seoul City and the Pink Ribbon Love Marathon was performed to provide donations for support of patients with cancer.

The Korea Breast Cancer Society is an academic society composed of scientists who conduct research on the etiology, epidemiology, diagnosis, and treatment of the disease. The society has always been the most active in leading cancer prevention campaigns compared to any other group in Korea. The Global Breast Cancer Conference organized by the Korean Breast Cancer Society (KBCS) has been held in conjunction with the 7th Biennial Meeting of the Asian Breast Cancer Society in Seoul, Korea. Not only academic activities but also social support by the KBCS members was encouraged.

A self-supported nation-wide group of breast cancer survivors is being developed in Korea. Korea Venus is a name of breast cancer survivors at Seoul National University Hospital and about 500 survivors have various activities. Similar self-supported groups are present in each hospital in Korea.

CONCLUSION

The war against cancer was declared in the U.S. by Nixon in 1971, and cancer mortality started to decline in 1991. The Japanese government initiated their National Cancer Control Plan in 1965, and National Cancer Screening Program for breast cancer was initiated in 1987. In Korea, major epidemiological studies to identify breast cancer risk factors were initiated about 20 years ago in the late the 1980s, and the fight against cancer was first declared by the Korean government in 1996. A national screening program against breast cancer was launched in 1999. The 5-year survival rate has increased in Korea during the last 15 years due to improvements in medical facilities, diagnosis and treatment, and the creation of the health insurance system. Thus, overall cancer mortality has started to decrease; however, the breast cancer death rate and incidence rates continue to increase today.

We have a final goal of fundamentally reducing the cancer mortality rate from the current 116.7 persons/100,000 in 2005 to 94.1 in 2015 (19.4%). We also strive to improve the 5-year survival rate in Korea from 45.9% in 2005 to 54% in 2015 during the second term of the National Cancer Control Plan. Since embarking on an economic development project in the early 1960s, Korea has achieved an incredible success that has dramatically transformed the Korean economy from an agricultural country into a highly advanced industrial nation during a relatively short period of time. Korea is now experiencing a rapidly ageing population, mainly due to increased life expectancy. Life expectancy for males is 75 years and that for females is 82 years. The system of universal healthcare coverage based on the national health insurance program was introduced in 1988 when the Seoul Olympic Games were held. An export-driven economic development strategy resulted in per capita gross national income from 87 USD in 1962 to 18,000 USD in 2006. Many aspects of women's health have also changed, but the statement that "a breast that has never lactated is more liable to become cancerous," as described by British doctor JE Lane-Claypon in 1926 is still true.

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