Breast cancer mortality is gradually increasing in Okinawa. The 1st Okinawa Breast Oncology Meeting was held on 6 July 2012 and discussions on how to curb the rising trend were focused on breast cancer screening, adjuvant treatment, socioeconomic and geographic issues, and the problem of complementary and alternative medicine. The consensus of the 1st Okinawa Breast Oncology Meeting was that ultrasonography screening is an acceptable screening system for Okinawan women because of the geographic disadvantage of having many small islands and rural areas. Educational and economic support is needed for women in rural areas to get correct information, for access to urban areas and to be treated by evidence-based optimal therapy for breast cancer. In addition, new approaches are needed for Okinawan people to successfully educate patients to correctly interpret evidence-based information.

**Key words:** breast cancer mortality — screening — adjuvant treatments — socioeconomic and geographic disadvantage — complementary and alternative medicine
Okinawa is east of Asia, at the southwest terminus of the great area of Japanese archipelago. Japan’s only island prefecture, Okinawa, includes a sweep of 160 islands, large and small, across 1000 km of ocean from east to west and 400 km from north to south. With its warm climate and lush nature, its special history and culture, Okinawa has so much to offer to visitors. As a premier destination, Okinawa attracts a host of visitors from mainland Japan and abroad. However, the average income per person in Okinawa is \( \sim 2,000,000 \) yen per year (70% of the average of Japanese income), which is the worst income in Japan. Maybe due to these geographic and economic disadvantages, Okinawa has now one of the worst breast cancer mortality rates in Japan (9). The ratio of breast cancer mortality has gradually increased as follows: 7.8 per 100,000 in 2007, 9.8 per 100,000 in 2008, 10.6 per 100,000 in 2009 and 12.5 per 100,000 in 2010 (9). Therefore, strong measures should be taken to reduce breast cancer mortality in Okinawa. This present paper summarizes the consensus of the 1st Okinawa Breast Oncology Meeting (the 1st OBOM) held on 6 July 2012. We discussed how to reduce breast cancer mortality in Okinawa, especially focusing on breast cancer screening, adjuvant treatment, socioeconomic and geographic disadvantages and complementary and alternative medicine (CAM).

**BREAST CANCER SCREENING**

A great deal of effort has been made to improve surgery, irradiation technique and chemoendocrine treatments for management of breast cancer, although the mortality rate of breast cancer is still high (10,11). The early detection of breast cancer is believed to be the best means of reducing this mortality, and mammography is the only evidence-based screening technology currently available for this purpose (10,11). Previous studies demonstrated that screening for breast cancer in asymptomatic women is estimated to reduce mortality by 20–35% (12,13). In the USA, by the year of 2000, \( \sim 70\% \) of women over the age of 40 years reported undergoing mammography in the previous 2 years (14). Western countries with national healthcare systems have state-sponsored breast cancer screening programs by mammography (11). Currently, the breast cancer screening rate in Japan was only 24.3% in 2010 (9) as opposed to 69.5% in 2005 in the UK and 81.9% in 2005 in the Netherlands (11). The breast cancer screening rate of Okinawan women was 29.2% in 2010 which was slightly better than the Japanese average (9). However, Okinawa includes a sweep of 160 islands, large and small, across 1000 km of ocean east-west and 400 km north-south and there is a geographic disadvantage for evidence-based breast cancer screening. As a consequence, breast cancer screening rates in Okinawa by modality were 74.1% for mammography and doctor palpation, 7.4% for MMG monodevice screening, 7.4% for US monodevice screening and 11.1% for other screening systems (Fig. 1). Although mammography is useful for detecting breast cancer in its early stages, it is thought that the effectiveness of mammography screening in women from 40 to 49 years of age is lower than that in women 50 years of age and over (2,15–17). The dense parenchyma in women before menopause can obscure tumor shadows and this results in the lower sensitivity of mammography screening in women 40–49 years of age (2,15,18). Ultrasonography is one of the candidates for the screening for younger women in order to find cancers at an early stage. Ultrasonography is able to detect breast cancer at an early stage based on the mass shape even in the dense parenchyma of women before menopause (15). The Ministry of Health, Labor and Welfare of Japan launched a national priority research program, entitled ‘Randomized controlled trial on effectiveness of ultrasonography for breast cancer screening’ in 2007 (19). To verify the quality and effectiveness of ultrasonography for breast cancer screening, 120,000 women aged 40–49 years will be enrolled, with randomization into two groups: mammography with ultrasonography vs. mammography alone (19). The first endpoints of this trial are sensitivity and specificity, and the secondary endpoint is the cumulative rate of advanced breast cancer in the two groups. Using the cancer registry is necessary to identify the false-negative cancer cases and accurately estimate the sensitivity of screening (19). Many rural areas in Okinawa are at a geographic disadvantage for breast screening by mammogram. Ultrasonography is smaller than the mammography device and is easy to transport to rural areas. Therefore, ultrasonography screening potentially might be an acceptable screening system for Okinawan women. In order to reduce the breast cancer mortality in Okinawa, the breast screening rate in Okinawa should be
increased, implementing various expedients to increase the screening rate, such as education and invitations to the public to raise awareness of the efficacy of breast screening.

**BREAST CANCER ADJUVANT TREATMENTS**

Breast cancer is not considered as a single disease. Breast cancer subtypes were defined by genome and histopathological immunohistochemistry (20–22). These subtypes have different epidemiological risk factors, different natural histories and different responses to systemic treatment (22–24). The St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011 strongly supported the clinicopathological determination of estrogen receptor expression, progesterone receptor expression, HER2 status and Ki-67 labeling index as useful for defining subtypes, and recommended that the clinicopathological markers were generally sufficient to guide therapeutic choice (22). Previous studies have demonstrated that taking tamoxifen for a recommended 5 years reduces the risk of recurrence or contralateral breast cancer 15 years after starting treatment (25). In addition, post-menopausal women should receive an aromatase inhibitor (26). Adjuvant treatment with letrozole, compared with tamoxifen, significantly reduces the risk of death, the risk of recurrent disease and the risk of recurrence at distant sites in post-menopausal women with hormone receptor positive breast cancer (26). As for chemotherapy, the factors for deciding chemotherapy were high histological grade, high Ki-67 labeling index, low hormone receptor expression, positive HER2 status and triple-negative invasive breast cancer (22). Patients with triple-negative breast cancer generally experience a more aggressive clinical course with increased risk of disease progression and poorer overall survival (27). Furthermore, this subtype accounts for a disproportionate number of disease-related mortality in part due to its aggressive natural history and/or lack of effective targeted agents beyond conventional cytotoxic chemotherapy (27). The addition of 1 year of adjuvant trastuzumab significantly improved disease-free and overall survivals among women with HER2-positive breast cancer (28). The results of a breast cancer mortality study in the Nahanishi Clinic Okinawa (N.T., Y.K., K.U. and K.T.), Okinawa Prefectural Chubu Hospital (M.G. and M.U.), Nakagami Hospital (H.Z. and M.O.) and Urasoe General Hospital (K.K. and K.M.) demonstrated that 11.6% of patients who died of breast cancer did not receive evidence-based adjuvant treatment including radiotherapy and chemoendocrine therapy. Previous studies demonstrated that adjuvant systemic treatments, including endocrine therapy for luminal A disease, chemoendocrine therapy for luminal B disease, the addition of anti-HER2 therapy for the presence of HER2-positive status and strict chemotherapy for triple-negative breast cancer, contribute to reduce breast cancer mortality (22–28). Some Okinawan breast cancer patients show early discontinuation and non-adherence to adjuvant treatments. Therefore, interventions to improve adherence and continuation of adjuvant therapies are needed for breast cancer patients in Okinawa.

**SOCIOECONOMIC AND GEOGRAPHIC DISADVANTAGE IN OKINAWA**

Socioeconomic status is one of the major determinants of health status and health disparities among different social and ethnic groups, and may serve as a health indicator that has a predictive value in spatial epidemiologic assessment (29). Previous studies demonstrated that substantial disparities in breast cancer survival were related to socioeconomic status as measured either at the individual or area levels (30–33). Factors that may mediate these disparities include the differences in the stage at diagnosis, access to and quality of care delivered and other correlates of low socioeconomic status (34). Women with less education and those who are unemployed, reside in a poor area or are uninsured or under-insured are more likely to be diagnosed as advanced and less likely to receive optimal treatments (35–37). Okinawa prefecture has the worst economic status in Japan (38). The average income per person in Japan was 2,965,000 yen in 2007, 2,756,000 yen in 2008 and 2,660,000 yen in 2009 (38). On the other hand, the income in Okinawa was 2,052,000 yen (69.2% of Japanese income) in 2007, 2,043,000 yen (74.2% of Japanese income) in 2008 and 2,045,000 yen (76.9% of Japanese income) in 2009 (Fig. 2) (38). Stage at diagnosis explained a large part of the socioeconomic status disparity in breast cancer mortality. A previous study demonstrated that this is likely because women living in the lowest socioeconomic status area had highest percent of advanced stage and worse survival for breast cancer (39). Lower financial resources are known to be associated with lower cancer screening rates, lack of or delayed follow-up and optimal treatment include operation, adjuvant chemoendocrine therapy and radiotherapy (39).

![Figure 2. Comparison of the average incomes per person in Japan and Okinawa in 2007, 2008 and 2009.](image-url)
suggested that one of the causes of the breast cancer mortality in Okinawa is the worse Okinawan socioeconomic status. Improving this unfortunate situation may lead to lower breast cancer mortality in Okinawan people. Geographic disadvantage is also suggested to be important for breast cancer mortality in Okinawa. Previous studies demonstrated that there is a consistent rural gradient in breast cancer incidence, being higher in major cities, and lower in more rural areas (40,41). On the other hand, survival tends to be lower for women living in more rural areas (40,41). Targeted interventions to increase breast cancer screening and treatment coverage in patients with lower socioeconomic status could reduce much of the socioeconomic disparity in breast cancer survival. The results of breast cancer mortality in the Nahanishi Clinic Okinawa (N.T., Y.K., K.U. and K.T.), Okinawa Prefectural Chubu Hospital (M.G. and M.U), Nakagami Hospital (H.Z. and M.O.) and Urasoe General Hospital (K.K. and K.M.) showed that 22.9% of breast cancer death patients were from rural areas, in which there were no hospitals, clinics and doctors with breast cancer specialties. In addition, many of these patients were advanced breast cancer stages at the first diagnoses (21.9% of Stage III and 35.4% of Stage IV) and were not treated with enough and optimal therapies for breast cancer (Fig. 3). Rural women may perceive less control over treatment decisions, and this may be due to limited access to information about options for breast cancer treatment. Rural cancer patients suffer greater psychological morbidity than do their urban counterparts and rural women report more unmet needs for help in dealing with fears about cancer recurrence. In addition, typically rural patients need to travel longer distances to access the diagnostic and treatment services, and this may be a disincentive to undertake the optimal treatments for breast cancer. This is particularly relevant when the treatments involve a prolonged absence from home resulting in disruptions to family life and financial hardship. Therefore, educational and economic supports should be needed for rural women to get correct information, to access to the urban area and to be treated with evidence-based and optimal therapies for breast cancer in Okinawa.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

The World Health Organization (WHO) defined CAM as a comprehensive term used to refer both traditional medical treatments and various forms of indigenous medicine (42). Cancer patients often use CAM such as nutritional supplements, psychological techniques and natural medical approach together with conventional medicine or in place of conventional therapy. The use of CAM in early stage breast cancer patients was regarded as a marker of greater psychosocial distress and a worse quality of life and advanced breast cancer patients used CAM to reduce higher levels of anxiety and pain (43,44). In Japan, >30% of cancer patients used CAM, and the most frequently used CAM involved natural products, such as mushrooms, shark cartilage and beewax-pollen mixtures (42,45,46). In addition, interactions between herbs and drugs may increase or decrease the pharmacologic or toxicologic effects of either component. Patients’ relatives, neighbors and friends often recommend that the patients use CAM in many situations. Of the total patients dying from breast cancer in Okinawa, 8.1% are mainly treated only with CAM. Traditionally, there are many prophets and/or fortune-tellers called ‘Yuta’ in Okinawa. Many Yuta encourage patients; however, some of them foretell bad fortune and recommend non-evidence-based products. In addition, because of the warm climate and lush nature in Okinawa, many CAM products such as seaweed products, wild grass tea, mushroom rooms and shark cartilage are produced in Okinawa. Therefore, Okinawan people tend to accept CAM products easily. The providers emphasize their effects on boosting the immune system based on basic experimental findings using cultured human tumor cells, and advertising through many magazines or through the internet with anecdotal reports of users (42). No reliable, well-designed clinical trials in cancer patients have been performed with these mushrooms (42). Nonetheless, many cancer patients used such products hoping for tumor growth suppression and cure rather than the complementary effect which is their permitted role (42). The patients’ lack of knowledge and errant beliefs about treatment and mistrust of the medical system are mutual factors associated with the underuse of effective adjuvant therapies. We have to improve cancer care by ensuring that discussion about adjuvant therapy includes a clear presentation of the benefits, not just the risks of treatment, and by addressing the patients’ feelings of trust and concern toward the medical system. Clearly, new approaches are needed to successfully educate patients on how to correctly interpret evidence-based information. Strategic efforts are needed for breast oncologists in Okinawa to provide this guidance.

CONCLUSION

Okinawa now has one of the worst rates of breast cancer mortality in Japan. The early detection of breast cancer is
believed to be the best means of reducing this mortality and mammography is the only evidence-based screening technology currently available for this purpose. However, many rural areas in Okinawa have geographic disadvantage for breast screening by mammogram. Ultrasonography screening is suggested to be an acceptable screening system for Okinawan women. Some breast cancer patients in Okinawa are not treated with the optimal adjuvant therapy because of their socioeconomic and geographic disadvantage. Educational and economic support is needed for women in rural areas to get correct information, to get physical access to urban areas and to be treated with evidence-based and optimal therapies for breast cancer in Okinawa. In addition, Okinawan people tend to accept CAM products easily. Therefore, new approaches are needed to successfully educate patients on how to interpret the presented information, and to base their decisions on correct and evidence-based information.

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Conflict of interest statement

None declared.

References

Appendix

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