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Perspective

Can We Improve Breast Cancer Mortality in Okinawa? : Consensus of the 7th Okinawa Breast Oncology Meeting

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The rate of breast cancer mortality in Okinawa has gradually been increasing up to 2010. Now Okinawa has the second worst mortality rate in Japan, in part due to the enormous dietary changes resulting from the post-World War II US military occupation, high incidence of obesity, high non-optimal treatment rate, and low breast-cancer screening rate. To reduce breast cancer mortality in Okinawa, we established the Okinawa Breast Oncology Meeting (OBOM) in 2012. At the 7th OBOM held on January 10th, 2014, we discussed the breast cancer mortality in Okinawa focusing on lifestyle, breast cancer screening and optimal treatments. The Okinawan women who were overweight and/or obese during premenopausal and postmenopausal ages had a statistically significant higher risk of breast cancer development compared to those with non-overweight and/or obese women. The traditional diet of Okinawa consists of foods low in calories but rich in nutritional value. Therefore, we recommend Okinawan people not to forget the Okinawan traditional lifestyle, and to reduce their bodyweight to prevent breast cancer. One of the main goals of the OBOM is to raise breast cancer screening attendance rates to 50% (29.2% in 2010). We should standardize the quality control for breast cancer screening in Okinawa. It is important to continue enlightening the Okinawan population to receive optimal treatment. In addition, we are striving to establish systematic medical cooperation between the hospitals specializing in breast cancer treatment with rural hospitals. The OBOM group endeavors to contribute to the improvement of breast cancer mortality in Okinawa.

Keywords: breast cancer mortality; complementary and alternative medicine; geographic disadvantage; lifestyle; screening
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Introduction

The rate of breast cancer mortality in Okinawa has been gradually increasing up to 2010 (Center for Cancer Control and Information Services, National Cancer Center, Japan 2013). The rate of breast cancer mortality in 2010 was 12.5 per 100,000, which was the second worst mortality rate in Japan (Center for Cancer Control and Information Services, National Cancer Center, Japan 2013; Tamaki et al. 2013). Strong measures should be taken to reduce breast cancer mortality in Okinawa. For this purpose, we established the Okinawa Breast Oncology Meeting (OBOM) in 2012 (Tamaki et al. 2013). We discussed on how to curb the rising trend, especially focusing on breast cancer screen-

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ing, adjuvant treatment, socioeconomic and geographic issues, and the problem of complementary and alternative medicine (CAM) (Tamaki et al. 2013). CAM is the term for medical products and practices that are not part of standard medical care. Traditionally, there are many prophets and/or fortunetellers in Okinawa. In addition, many CAM products are produced in Okinawa. Therefore, Okinawan people tend to accept CAM products easily.

Can we improve breast cancer mortality in Okinawa? The 7th OBOM was held on January 10th, 2014, and 15 breast oncologists participated in the 7th OBOM (see Appendix). We discussed the breast cancer mortality in Okinawa focusing on lifestyle, breast cancer screening and optimal treatments. We analyzed the data of dying from breast cancer between 2009 and 2012 from 6 hospitals in Okinawa (Nahanishi Clinic, Nakagami Hospital, Urasoe General Hospital, Okinawa Prefectural Chubu Hospital, Heartlife Hospital and Tomishiro Central Hospital).

Lifestyle

Many previous studies have demonstrated that obesity increased breast cancer risk in postmenopausal women but decrease the risk in premenopausal women (Loi et al. 2005; Palmer et al. 2007; Mathew et al. 2008). However, there are a few previous studies demonstrating that there is positive correlation between obesity and breast cancer incidence in both premenopausal and postmenopausal women (Sonnenschein et al. 1999; Tehard and Clavel-Chapelon 2006). Obesity is a growing health problem globally and this trend has been especially marked among individuals living in Okinawa compared to individuals living in mainland Japan (Matsushita et al. 2008). The longevity advantage has been well documented because of the traditional lifestyle in Okinawa (Suzuki et al. 2001; Willcox et al. 2007; Matsushita et al. 2008). However, enormous dietary changes resulting from the post-World War II US military occupation of Okinawa has had largely deleterious health effects, with Okinawan people developing higher rates of obesity corresponding to these post-war years (Todoriki et al. 2004; Willcox 2005; Tamaki et al. 2013). The introduction of the US lifestyle and diet to people of Okinawa is generally considered the simplest and most plausible explanation of the clearly documented loss of longevity advantage among younger generations of Okinawan people (Todoriki et al. 2004; Willcox 2005; Tamaki et al. 2013). We reported on the correlation between BMI and breast cancer risk for Okinawan people and in particular increased risks associated with the marked increment of BMI since US military occupation in our previous study (Tamaki et al. 2014). Results of this study demonstrated that the Okinawan women who were overweight and/or obese during premenopausal and postmenopausal ages had a statistically significant higher risk of breast cancer development compared to those with non-overweight and/or obese women (Tamaki et al. 2014). The Okinawan people have adjusted to low calorie environment for more than a millennium in a rather isolated island environment (Tamaki et al. 2014). Thus, this increment of breast cancer development in Okinawan women following World War II might be explained by the introduction of an US style diet as a result of the US military occupation, oversaturation by lipids and cholesterol of the liver clearance system of estrogen in Okinawan overweight women, expose their system to much endogenous estrogen (Tamaki et al. 2014). In addition, the peak ages of the age-adjusted incidence rates in Okinawa were 50-54 years old (61.8/100,000) in 1998, 55-59 years old (129.6/100,000) in 2003 and 65-69 years old (192.7/100,000) in 2008, respectively (Okinawa Prefectural Institute of Health and Environment 2014). The age-adjusted breast cancer incidence rate and the peak age have been increasing in Okinawa during these years, and these trends have been generally similar to the tendency in the USA (Okinawa Prefectural Institute of Health and Environment 2014; Saika and Sobue 2009). Therefore, we recommend Okinawan people not to forget the Okinawan traditional lifestyle, and to reduce their bodyweight.

Breast Cancer Screening

The early detection of breast cancer is believed to be the best means of reducing mortality (Suzuki et al. 2008; Kawai et al. 2009). The results from the 6 prominent hospitals in Okinawa shows that the numbers of patients dying from breast cancer between 2009 and 2012 were 10 for Stage I, 61 for Stage II, 41 for Stage III and 62 for Stage IV at the first diagnoses (Fig. 1). If more of them had received breast cancer screening, we may have diagnosed them at an earlier stage cured more patients. The breast cancer screening rates in Okinawa were 27.0% in 2007 and 29.2% in 2010 (Center for Cancer Control and Information Services, National Cancer Center, Japan 2013). In contrast, about 70% of women over the age of 40 years reported undergoing mammography in the United States of America (Swan et al. 2003). To reduce breast cancer mortality in Okinawa, increasing these low attendance rates has become an impor-

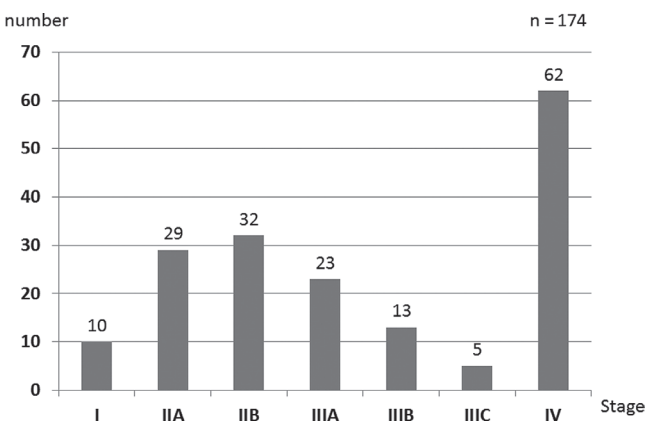

Fig. 1. The numbers of patients died of breast cancer between 2009 and 2012.
Total 174 patients were categorized, based on the stages of breast cancer at the first diagnoses.

tant issue. Therefore, one of the main goals of the OBOM is to raise breast cancer screening attendance rates to 50%. In addition, it is also important to improve the accuracy of breast cancer screening. Concerning recall rates, depending on the age of the women screened and the screening round, generally about 5% of women screened are recalled for assessment (NHS Cancer Screening Programmes 2004). The minimum National Health Service Breast Screening Programme (NHSBSP) in United Kingdom standard is that no more than 10% of women screened for the first time or 7% of women who have been screened before should be recalled for assessment (NHS Cancer Screening Programmes 2005). According to the Japan Cancer Society, the recall rate in Japan was 6.2% in 2010 (NHS Cancer Screening Programmes 2005). On the other hand, the recall rates in Okinawa varied from 5% to 20% by screening center. This prompted the 1st Naha Medical Association Breast Screening Quality Control meeting to standardize the quality control for breast cancer screening in Okinawa on April 14th, 2014.

Optimal Treatment

Among 174 patients died from breast cancer, 103 patients (59%) were at Stage III and Stage IV on the first diagnoses in our series (Fig. 1). Many previous studies have demonstrated that early detection is the best means for reducing breast cancer mortality (Suzuki et al. 2008; Kawai et al. 2009). However, our data revealed that patients at Stage I and II account for 40% of those dying from breast cancer. The reason for the suboptimal results may be that these patients show discontinuation and non-adherence to adjuvant treatments. Fig. 2 shows the rate of patients receiving optimal treatment or not. Among the 174 patients, 40 patients (23%) did not receive optimal treatment because of their rejection of treatment, wrong knowledge and geographic disadvantage.

Traditionally, there are many soothsayers and/or fortunetellers called 'Yuta' in Okinawa. Many Yuta encourage patients; however, some of them foretell a bad fortune and recommend non-evidence-based products (Tamaki et al. 2013). In addition, because of the warm climate and lush foliage in Okinawa, many CAM products such as seaweed products, wild grass tea, mushrooms and shark cartilage are produced in Okinawa (Tamaki et al. 2013). Therefore, Okinawan people tend to accept CAM products easily. Patients' relatives, neighbors and friends often recommend that the patients use CAM in many situations (Tamaki et al. 2013). The results of a previous study demonstrated that of the total patients dying from breast cancer in Okinawa, 8.1% are mainly treated only with CAM (Tamaki et al. 2013). It is important to educate patients on how to correctly interpret evidence-based information. We started "Okinawa-no-Sumizumi project" to propagate the correct breast cancer information to the people of Okinawa. We held 24 lectures in urban and rural areas relating to breast cancer, on how to interpret evidence-based information

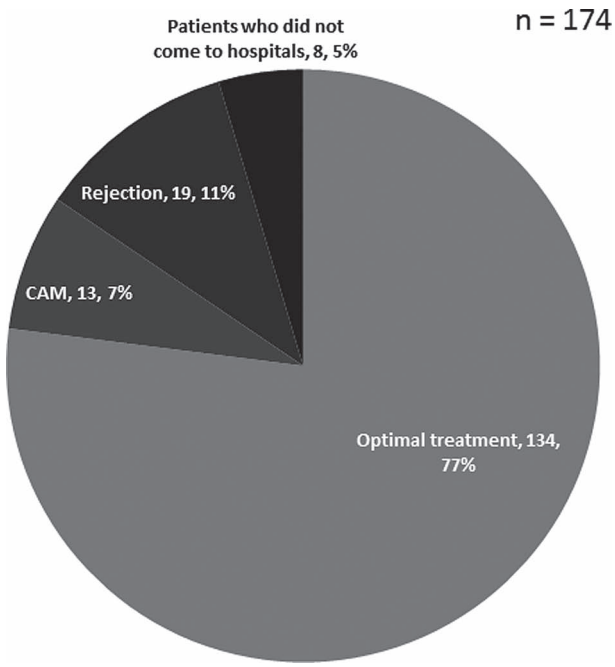

Fig. 2. Treatment choice of patients died of breast cancer in Okinawa.
Note that 40 patients (23%) did not receive optimal treatment.

including breast cancer screening, prevention and optimal treatments. It is important to continue this work of enlightening the Okinawan population on optimal treatment option in breast cancer treatments.

Geographic disadvantage is also suggested to be an important factor of disparity for breast cancer mortality in Okinawa. We showed in a previous study Okinawa includes a sweep of 160 islands, large and small, across 1,000 km of ocean from east to west and 400 km from north to south (Tamaki et al. 2013). As such, this is disadvantage of medical environment for Okinawan people. There are 13 breast cancer specialists in Okinawa, which is a slightly higher rate than the Japanese average (9.2 per 1,000,000 in Okinawa and 8.9 per 1,000,000 in Japan). However, all of the specialists work in urban areas; 6 in the capital city of Naha, 3 in Urasoe (5.59 km from Naha), 2 in Tomigusuku (5.77 km from Naha), 1 in Nishihara (8.82 km from Naha) and 1 in Okinawa city (18.55 km from Naha), respectively. There are no specialists in the northern area of mainland Okinawa and the distant island areas. Probably as a result, women in these areas show early discontinuation and non-adherence to adjuvant treatments. Rural women may perceive themselves to have less control over treatment decisions, and this may be due to limited access to information about options for breast cancer treatment. Therefore, economic support should be given to rural women to access urban areas so that they can be treated with evidence based and optimal therapies for breast cancer in Okinawa. In addition, it is very important to establish systematic medical cooperation between the hospitals specializing in breast

cancer treatment and rural hospitals. Recently, we initiated new medical cooperation efforts with a prefectural hospital in Miyako island (287.37 km from Naha) and 3 hospitals in Ishigaki island (411.36 km from Naha). We expect to improve the current unfortunate situation and lower breast cancer mortality in rural areas.

Conclusion

The ratio of breast cancer mortality in Okinawa has gradually decreased from 2010 through 2012 (12.5 per 100,000 in 2010, 11.5 per 100,000 in 2011 and 9.6 per 100,000 in 2012, respectively). However, the goal of the OBOM group is 0 percent breast cancer mortality. Therefore, we are continuing our effort to reduce breast cancer mortality in Okinawa. The recommendation of the 7th OBOM is summarized below.

1. We recommend Okinawan people not to forget Okinawan traditional lifestyle, and to reduce their body-weight to prevent breast cancer occurrence.

2. One of the main goals of OBOM is to raise breast cancer screening attendance rates to 50%.

3. We should standardize the quality control for breast cancer screening in Okinawa.

4. It is important to continue enlightening the Okinawan population to receive optimal evidence based treatment.

5. We try to establish medical cooperation between the hospitals specialized in breast cancer treatment and rural hospitals.

We, the OBOM group, are working hard to contribute to decreasing the breast cancer mortality in Okinawa.

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Conflict of Interest

The authors declare no conflict of interest.

References

Center for Cancer Control and Information Services, National Cancer Center, Japan (2013) [*Updated*: May 18, 2012] http://ganjoho.jp/professional/statistics/statistics.html [*Accessed*: January 31, 2015].

Kawai, M., Kuriyama, S., Suzuki, A., Nishino, Y., Ishida, T., Ohnuki, K., Amari, M., Tsuji, I. & Ohuchi, N. (2009) Effect of screening mammography on breast cancer survival in comparison to other detection methods: a retrospective cohort study. *Cancer Sci.*, **100**, 1479-1484.

Loi, S., Milne, R.L., Friedlander, M.L., McCredie, M.R., Giles, G.G., Hopper, J.L. & Phillips, K.A. (2005) Obesity and outcomes in premenopausal and postmenopausal breast cancer. *Cancer Epidemiol. Biomarkers Prev*., **14**, 1686-1691.

Mathew, A., Gajalakshmi, V., Rajan, B., Kanimozhi, V., Brennan, P., Mathew, B.S. & Boffetta, P. (2008) Anthropometric factors and breast cancer risk among urban and rural women in South India: a multicentric case-control study. *Br. J. Cancer*, **99**, 207-213.

Matsushita, Y., Takahashi, Y., Mizoue, T., Inoue, M., Noda, M. & Tsugane, S. (2008) Overweight and obesity trends among Japanese adults: a 10-year follow-up of the JPHC Study. *Int. J. Obes*., **32**, 1861-1867.

NHS Cancer Screening Programmes (2004) Changing Lives: NHS Breast Screening Programme 2004 Annual Review.

NHS Cancer Screening Programmes (2005) Consolidated Guidance on Standards for the NHS Breast Screening Programme: NHSBSP Publication No 60.

Okinawa Prefectural Institute of Health and Environment (2014) http://www.eikanken-okinawa.jp/index.htm [*Accessed*: January 31, 2015].

Palmer, J.R., Adams-Campbell, L.L., Boggs, D.A., Wise, L.A. & Rosenberg, L. (2007) A prospective study of body size and breast cancer in black women. *Cancer Epidemiol. Biomarkers Prev*., **16**, 1795-1802.

Saika, K. & Sobue, T. (2009) Epidemiology of breast cancer in Japan and the US. *JMAJ*, **52**, 39-44.

Sonnenschein, E., Toniolo, P., Terry, M.B., Bruning, P.F., Kato, I., Koenig, K.L. & Shore, R.E. (1999) Body fat distribution and obesity in pre- and postmenopausal breast cancer. *Int. J. Epidemiol.,* **28**, 1026-1031.

Suzuki, A., Kuriyama, S., Kawai, M., Amari, M., Takeda, M., Ishida, T., Ohnuki, K., Nishino, Y., Tsuji, I., Shibuya, D. & Ohuchi, N. (2008) Age-specific interval breast cancers in Japan: estimation of the proper sensitivity of screening using a population-based cancer registry. *Cancer Sci*., **99**, 2264-2267.

Suzuki, M., Wilcox, B.J. & Wilcox, C.D. (2001) Implications from and for food cultures for cardiovascular disease: longevity. *Asia Pacific J. Clin. Nutr.*, **10**, 165-171.

Swan, J., Breen, N., Coates, R.J., Rimer, B.K. & Lee, N.C. (2003) Progress in cancer screening practices in the United States: results from the 2000 National Health Interview Survey. *Cancer*, **97**, 1528-1540.

Tamaki, K., Tamaki, N., Kamada, Y., Uehara, K., Zaha, H., Onomura, M., Gushimiyagi, M., Kurashita, K., Miyazato, K., Tengan, H., Miyara, K. & Ishida, T. (2013) The challenge to reduce breast cancer mortality in Okinawa: consensus of the first Okinawa breast oncology meeting. *Jpn. J. Clin. Oncol*., **43**, 208-213.

Tamaki, K., Tamaki, N., Terukina, S., Kamada, Y., Uehara, K., Arakaki, M., Miyashita, M., Ishida, T., McNamara, K.M., Ohuchi, N. & Sasano, H. (2014) The correlation between body mass index and breast cancer risk or estrogen receptor status in Okinawan women. *Tohoku J. Exp. Med.*, **234**, 169-174.

Tehard, B. & Clavel-Chapelon, F. (2006) Several anthropometric measurements and breast cancer risk: results of the E3N cohort study. *Int. J. Obes.*, **30**, 156-163.

Todoriki, H., Willcox, D.C. & Willcox, B.J. (2004) The effect of post-war dietary change on longevity and health in Okinawa. *Oki. J. Amer. Studies*, **1**, 52-61.

Willcox, B.J., Willcox, D.C., Todoriki, H., Fujiyoshi, A., Yano, K., He, Q., Curb, J.D. & Suzuki, M. (2007) Caloric restriction, the traditional Okinawan diet, and healthy aging: the diet of the world's longest-lived people and its potential impact on morbidity and life span. *Ann. NY Acd. Sci.*, **1114**, 434-455.

Willcox, D.C. (2005) Okinawa longevity: where do we go from here? *Nutr. Dietetics*, **8**, 9-17.

Appendix

The 7th OBOM members.

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