

# Trends of breast cancer treatment in Sabah, Malaysia: a problem with lack of awareness

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## ABSTRACT

**Introduction:** Sabah, formerly known as North Borneo, is part of East Malaysia. 52.2 percent of patients with breast cancer in Sabah presented at advanced stages and up to 20.4 percent of patients defaulted proper treatment, opting for traditional therapy. We performed a two-year prospective study looking at the treatment trends of breast cancer in Sabah.

**Methods:** Our subjects were all newly-diagnosed breast cancer cases seen at the hospital in 2005 and 2006. Type of surgery, chemotherapy, radiotherapy, hormonal therapy and surgical complication for each patient were studied.

**Results:** Out of 186 newly-diagnosed cases, 152 (81.7 percent) had surgery, 126 (67.7 percent) had chemotherapy, 118 (63.4 percent) had radiotherapy and 92 (49.5 percent) had hormonal therapy. 18.3 percent did not have surgery either due to refusal of treatment or advanced disease. They were more likely to be non-Chinese (91.1 percent, p-value is 0.02). Only 15.8 percent had breast-conserving surgery. The most frequent surgical complication was seroma formation (15.0 percent). The commonest chemotherapy regime and hormonal therapy were anthracycline-based regime (88.1 percent) and tamoxifen (95.8 percent), respectively.

**Conclusion:** The proportion of breast-conserving surgery and usage of modern adjuvant therapies are low in Sabah. This can be attributed to lack of breast cancer awareness leading to late presentation and refusal of treatment, coupled with insufficient health service funding.

**Keywords:** advanced cancer, breast cancer, cancer awareness, cancer treatment

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Fig. 1 Photograph shows a patient with locally advanced breast cancer.

## INTRODUCTION

Management of breast cancer has evolved and progressed tremendously over the past few decades. This has translated into improved survival of breast cancer patients which was observed worldwide. Breast-conserving surgery is now regarded an oncologically-safe procedure. A 20-year follow-up demonstrated no difference in long-term survival rates between breast-conserving surgery and mastectomy, although the locoregional recurrence rates appear to be somewhat higher for breast-conserving treatment than mastectomy.<sup>(1,2)</sup> The advent of aromatase inhibitors, such as anastrozole, letrozole and exemestane, has created a new paradigm in the management of oestrogen receptor (ER)-positive breast cancer in postmenopausal women. Various studies revealed that the usage of aromatase inhibitors, either as primary or extended adjuvant hormonal therapy, conferred better disease-free survival compared to tamoxifen alone.<sup>(3-6)</sup> The addition of taxanes, such as docetaxel, to the anthracycline-based chemotherapy regime also conferred better disease-free and overall survival compared to the anthracycline-based regime alone.<sup>(7)</sup> Besides, the introduction of targeted therapy with a monoclonal antibody, such as trastuzumab, offers an effective adjuvant therapy in the treatment of HER2-overexpressing breast cancer.<sup>(8,9)</sup>

Breast cancer is the commonest cancer among

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**Table I. Types of surgical treatment in the study population.**

Surgery	No. (%) of cases
Mastectomy	129 (69.4)
Quadrantectomy	3 (1.6)
Lumpectomy	19 (10.2)
Hookwire-guided excision	1 (0.5)
Breast reconstruction	0
No surgery	34 (18.3)

Malaysian women with an overall age-standardised risk of 46.2 per 100,000.<sup>(10)</sup> A Malaysian woman has a one in 20 chance to develop breast cancer in her life time. As with most Asian countries, there is no national breast cancer mammographic screening programme in our country. In Sabah, women with breast cancer present late. 52.2% of patients presented with advanced disease (36.6% with locally advanced and 15.6% with metastatic disease) and they are more likely to be non-Chinese, poor, non-educated and from a rural area (Fig. 1).<sup>(11)</sup> Sabah, formerly known as North Borneo, is part of East Malaysia and is the second largest state in Malaysia. The largest indigenous ethnic group is the Kadazan-Dusun (17.8%), followed by Bajau (13.5%), Malay (11.5%), Murut (3.3%) and others (14.6%). The largest non-indigenous ethnic group is the Chinese (9.6%) while other non-indigenous groups make up 4.8% of the population. Nearly 25% of the population is made up of non-Malaysians (mainly Filipinos and Indonesians). Despite being the second largest state, Sabah has the poorest healthcare service in Malaysia with a doctor to population ratio of 1:2,938 (in 2005).<sup>(12)</sup> The latest published National Cancer Registry of Malaysia data on breast cancer did not include data from Sabah due to underreporting of cases. To date, there are 14 general surgeons, two plastic surgeons and one oncologist in the public health service covering the care of 3.39 million people in Sabah.<sup>(12)</sup>

Queen Elizabeth Hospital, situated at Kota Kinabalu, the capital of Sabah, is the main public tertiary referral centre in the state. We adopt the triple assessment approach, namely clinical, radiological and cytological/histological assessment, for patients who present to us with a breast complaint. Palpable breast lumps will either be biopsied by fine-needle aspiration cytology (FNAC) or core needle histology, depending on the size of lesion. Suspicious palpable lesions which could not be adequately diagnosed with either FNAC or core-needle biopsy histology will be excised histological examination. Impalpable suspicious lesions from radiological assessments will either be biopsied by radiological-guided fine-needle aspiration, core-needle biopsy or hookwire-guided excision. The

decision for mastectomy or breast-conserving surgery will be made depending on the size of lesion and the patient's decision. As there is limited expertise and resources, sentinel lymph node biopsy and frozen section are not practised in our centre. We routinely perform axillary clearance for breast cancer patients except for carcinoma *in situ* or mastectomy for palliation. Neo-adjuvant and adjuvant chemotherapy and radiotherapy are both managed by the oncology unit of the hospital. Preoperative counselling is conducted by a nursing staff at the breast clinic. There is also a breast cancer support group run and funded by a non-governmental organisation to support patients especially during the postoperative period. In addition, there is a well-structured palliative care unit in the hospital for patients with metastatic disease.

We conducted a two-year prospective study in this hospital to look at the trends of management of breast cancer including type of surgery, chemotherapy, radiotherapy, hormonal therapy and surgical complication, which were subsequently compared with data from the rest of Malaysia as well as globally. Approval from the hospital director's office was obtained before the study was initiated. We hope that a clearer picture on the trends of management of breast cancer in Sabah will lead to measures which can be taken to improve the outcome of management of the disease in Sabah as well as Malaysia as a whole.

## METHODS

The subjects of our study were all newly-diagnosed breast cancer patients seen in the Queen Elizabeth Hospital, Kota Kinabalu, Malaysia, from January 2005 to December 2006. We included patients who were referred from private and other public institutions for further management of breast cancer, but excluded patients who refused to participate in the study. The patients' data including race, age, background, stage at presentation, tumour hormonal status, type of surgery, chemotherapy regime, hormonal therapy given and possible secondary complications, was collected and analysed. A standardised structured questionnaire was developed and used for the interview and data collection. Staging of the disease was in accordance to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, sixth edition.<sup>(13)</sup> Advanced breast cancer (locally advanced and metastatic disease) is defined as breast cancer at either Stage III or IV of the disease. The Statistical Package for the Social Sciences version 15.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Chi-square test was used for associations between categorical variables. The level of statistical significance was set at  $p < 0.05$ .

**Table II. Surgical treatment for early breast cancer, locally advanced breast cancer and metastatic breast cancer.**

Breast cancer stage	Total no. of cases	Mastectomy, no. (%)	Breast-conserving surgery, no. (%)	No surgery, no. (%)
Early breast cancer	89	63 (70.8)	20 (22.5)	6 (6.7)
Locally advanced breast cancer	69	58 (84.1)	1 (1.4)	10 (14.5)
Metastatic breast cancer	28	8 (28.6)	2 (7.1)	18 (64.3)
Total	186	129 (69.3)	23 (12.4)	34 (18.3)

## RESULTS

A total of 186 newly-diagnosed breast cancers were seen during the study period. No patient refused to participate in the study. The commonest age group seen was 40–49 years (32.3%), with a mean age of 51.0 (standard deviation 11.0) years. Infiltrating ductal carcinoma was the commonest histological type (88.4%), followed by ductal carcinoma *in situ* in 4.3%, invasive lobular carcinoma in 3.2%, mucinous carcinoma in 2.7%, medullary carcinoma in 2.2%, papillary carcinoma in 1.6% and apocrine tumour in 0.5%. The commonest mode of presentation was with a breast lump, seen in 78.0% of patients, while 9.1% of patients presented with an ulcerative mass and only 2.2% presented with suspicious lesion on mammography. 3.2% of patients presented with symptoms of metastasis which include jaundice, bone and abdominal pain. The commonest pathological stage of breast cancer at presentation in our institution was Stage III at 36.6%, followed by Stage II at 30.1%, Stage IV at 15.6%, Stage I at 12.9%, and Stage 0 at only 4.8%. 59.1% of tumours were ER-positive and 54.8% were progesterone receptor (PR) positive. HER2 receptor status was not routinely performed in our institution during the study period due to inadequate funding and was therefore not included as part of our study.

Of the 186 patients, 152 (81.7%) had surgery. 69.4% of total patients had mastectomy with or without axillary clearance and only 12.3% had breast-conserving surgery (Table I). 34 (18.3%) patients did not have any form of surgery, either due to advancement of the disease or treatment was refused. 91.1% of this group of patients are non-Chinese ( $p = 0.02$ ). Among 89 patients presenting with early breast cancer, 63 (70.8%) had mastectomy, 20 (22.5%) had breast-conserving surgery and six (6.7%) did not have surgery. Patients with locally-advanced breast cancer were offered either surgery or neo-adjuvant chemotherapy, depending on tumour operability. Large wound defects which could not be directly closed were covered with split skin grafts. In general, 84.1% of patients with locally-advanced breast cancer had mastectomy. Only 1.4% had breast-conserving surgery and 14.5% did not have any surgery done. Among patients who presented

**Table III. Stages at which patients defaulted treatment.**

Treatment stage	No. (%) of cases
Operation	21 (55.3)
Chemotherapy	11 (28.9)
Radiotherapy	5 (13.2)
Post-treatment follow-up	1 (2.6)

with metastatic disease, eight (28.6%) had mastectomy, two (7.1%) had breast-conserving surgery and 18 (64.3%) did not have surgery done (Table II). Due to the limitation of plastic and reconstruction service in our centre, breast reconstruction for mastectomy was not usually offered to patients. No breast reconstruction was performed during the study period. The commonest post-mastectomy complication was seroma formation (14.8%). This was followed by wound dehiscence (8.2%), lymphoedema (7.4%), flap necrosis (3.3%) and nerve injury (1.6%).

126 (67.7%) patients underwent chemotherapy; 111 (88.1%) had an anthracycline-based regime, 11 (8.7%) had a taxane-based regime, three (2.4%) had a cyclophosphamide, methotrexate and 5-fluorouracil regime, and one (0.8%) had oral capecitabine. A typical anthracycline-based chemotherapy regime comprises six cycles of 5-fluorouracil, epirubicin and cyclophosphamide. Of the 129 patients who had mastectomy, 96 (74.4%) had radiotherapy. Radiotherapy was delivered in 20 fractions of a total of 45 Gy by a linear accelerator radiotherapy machine. This service was provided by a local private medical centre through government sponsorship as the service is not available in our centre. It is important to report that out of the 23 patients who had breast-conserving surgery, only 18 (78.3%) had radiotherapy. Despite proper counselling on the necessity of radiotherapy post breast-conserving surgery, five (21.7%) patients refused radiotherapy. 110 (59.1%) patients had an ER-positive tumour and 96 patients were put on hormonal therapy. 13 patients refused treatment and another patient succumbed to the disease before treatment could be initiated. Of 96 patients who were given hormonal therapy, 92 (95.8%) had tamoxifen and only four (4.2%) had aromatase inhibitor (either anastrozole or letrozole).

In our study, a total of 38 (20.4%) patients refused the proper recommended treatment or defaulted follow-up altogether with the majority of them opting for traditional or alternative therapy. The commonest stage of treatment that patients defaulted was operative intervention (55.3%) (Table III). As with advanced disease at presentation,<sup>(11)</sup> factors associated with refusal of treatment and follow-up were: non-Chinese race (24% vs. 12%), rural residence (24% vs. 17%), poverty (monthly income < RM 1,000) (24% vs. 16%) and having no education (27% vs. 17%). However, these findings did not reach statistical significance, likely due to the small sample size.

## DISCUSSION

The proportion of breast cancer patients being treated with breast-conserving surgery, modern chemotherapy and hormonal modulating agents is low in Sabah. A significant portion of the patients in our study did not have surgery at all. This was secondary either to refusal of surgery or advanced disease. 91.1% of this group of patients were non-Chinese ( $p = 0.02$ ). In our study, mastectomy was the commonest surgery performed (69.4%). Only 12.3% of the patients had breast-conserving surgery and no patient had breast reconstruction surgery during our study period. As expected, breast-conserving surgery was more commonly performed in early breast cancers (22.5%) compared to locally advanced disease (1.4%) and metastatic disease (7.1%). University Malaya Medical Centre, Kuala Lumpur, has a breast-conserving surgery rate of 27%.<sup>(14)</sup> This is further compared to centres in other more developed countries such as Asan Medical Centre in Korea (39.1%), Australian Capital Territory and South-Eastern New South Wales breast cancer treatment group in Australia (47%) and Worcestershire Acute Hospitals National Health Service Trust in the United Kingdom (36.1%–54.9%).<sup>(15-17)</sup> The practice of breast-conserving surgery in Sabah is limited by the lack of expertise, advanced disease at presentation, smaller breast volume of Sabahan women compared to their Western counterparts, and possibly the preference of many Sabahan women for mastectomy due to locoregional recurrence concerns rather than cosmetic concerns. Mastectomy will also make subsequent treatment and follow-up easier, especially for patients from rural areas. Usage of modern chemotherapy and hormonal modulating agents is limited by the cost of the medication coupled with insufficient healthcare funding. Most patients are poor and could not afford these expensive medications.

It is very disappointing to discover that 20.4% of the patients in our study defaulted proper treatment and follow-up; most opted for alternative or traditional therapy. This further delayed appropriate treatment.

Most of them returned with more advanced disease after such treatment had failed. The commonest treatment refused by the patient was surgery (55.3%). We did not find any statistically significant factors associated with patients defaulting treatment. Lack of awareness of breast cancer among women in Sabah and a strong influence of traditional and cultural beliefs among patients are the main attributing factors. A lack of awareness with a wrong social and cultural perception of breast cancer have been associated with advanced disease at presentation.<sup>(18,19)</sup> Sabah women feel that their role as a wife, mother and female as a whole will be seriously jeopardised if they have breast cancer. They are worried that their husbands will leave them and their children will love them less as a mother. Thus, a strong sense of denial will normally develop as a protective mechanism against such a threat. Some also may be misinformed that mastectomy is the only surgical option, and they fear that surgery will disturb the tumour and cause it to grow and spread faster. It is also not uncommon to see patients who were not bothered by a painless enlarging breast lump which they regarded as non-cancerous. Due to a strong traditional influence and fear of surgery, many women will initially seek traditional or alternative treatment, such as “bomoh” or faith healing, before they present to the hospital. It was reported by Taib et al that between 15.5% and 45.3% of Malaysian women with breast cancer sought traditional treatment before attending the breast clinic.<sup>(20)</sup> Thus it is not surprising to have so many patients presenting with ulcerative lesions and metastatic disease. Traditional and alternative therapies are freely available in Malaysia. Advertisement boards and banners promoting such therapies can easily be seen at common public places in Malaysia.

More effort is needed to increase the awareness of breast cancer among women in Sabah. The month of October is breast cancer awareness month in Malaysia and effort must be made to involve women in rural areas, as most patients with advanced cancer are from these areas.<sup>(11)</sup> The media and non-government organisations can play an invaluable role in such efforts. Hospitals and health clinics in rural areas should also multiply efforts to educate and promote breast cancer awareness, including the practice of breast self-examination among the villagers and enable them to be more “breast aware”. Practice of breast self-examination is generally low in Malaysia. In a study by Chan, from a total of 1,303 women registered and attending a Malaysian well person’s clinic programme at Hospital Ipoh, Malaysia, only 1.3% (17 patients) practised breast self-examination regularly and only 2.9% of the 207 women with a past or family history of other cancers practised breast self-examination regularly.<sup>(21)</sup>

The public should also be well informed that alternative and traditional therapies are ineffective and have no place in the management of breast cancer. The practice of alternative and traditional medicine should be regulated and monitored strictly. Poor road conditions and communication network to rural areas in the state should be improved to facilitate referrals and delivery of more effective healthcare. Increasing the number of general and plastic surgeons, and developing specialties such as breast surgery, radiology, pathology and oncology in Sabah should be given priority. Setting up a national mammographic breast cancer screening programme is desirable. In addition, continuing medical education in breast cancer among general practitioners, clinicians and other healthcare professionals should take place regularly. As clinical breast examination (CBE) may play a positive role in detecting cancer earlier, especially in reducing tumour size from 5 cm to 2 cm at presentation in developing countries without a mammography screening programme,<sup>(20)</sup> the practice of CBE by doctors and trained nurses should be encouraged. There should be a larger allocation of funds for the use of modern chemotherapy and hormonal therapy, such as taxanes, trastuzumab and aromatase inhibitors. A fast-track referral system for patients suspected of breast cancer to be seen earlier at referral hospitals should also be formally put in place.

In conclusion, the majority of women with breast cancer in Sabah presented with advanced disease, and a significant portion of them defaulted proper treatment and held a strong belief in the effectiveness of alternative and traditional treatments. The practice of breast-conserving surgery, usage of modern chemotherapy and hormonal treatments is low in Sabah. More effort is needed to increase the awareness of breast cancer among women in Sabah, especially among those who are more likely to present with advanced disease. Healthcare professionals, the government and non-government organisations should collaborate and take up active roles to generate such awareness, and improve the healthcare service, communication system and standard of treatment of breast cancer in Sabah.

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