RESEARCH ARTICLE

Evaluation of Eligibility and Utilization of Breast Conservation Treatment in an Asian Context

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Abstract

Background: Breast conservation treatment (BCT) has long been recognised to provide survival outcomes equivalent to mastectomy for the treatment of breast cancer. However, published reports of BCT rates in Asian communities are lower than those from Western countries. This study sought to investigate the eligibility and utilisation of BCT in a predominantly Asian population. Materials and Methods: All patients treated surgically by a single surgeon at a private medical facility between 2009 and 2011 were included in the study. Patients were deemed to have successful BCT if they underwent breast conserving surgery with pathologic clear margins and completed all recommended adjuvant treatment. Those who did not complete adjuvant treatment were excluded from the analysis. Results: Data from a total of 161 patients who underwent treatment during the study period were analysed. The mean age was 48.8 years. One hundred and six patients (65.8%) were of Chinese ethnicity, 12 were Indian (7.5%), 11 were Malay (6.8%), 18 were Caucasian (11.2%) and 14 (8.7%) were of other Asian ethnicity. One hundred and thirty-eight women (85.7%) underwent BCT. Of the 23 (14.3%) who underwent mastectomy, 8 (5.4%) elected to undergo a mastectomy despite being eligible for BCT. In total, it was assessed that 146 of 161 patients (90.7%) were eligible for BCT and utilisation was 94.5%. Conclusions: In this study, eligibility, utilisation of BCT and eventual successful breast conservation rates are similar to published rates in Western communities. Additional research is needed to investigate the reasons for the lower published BCT rates in Asian countries and determine ways to improve them.

Keywords: Breast conservation treatment eligibility utilisation oncoplastic breast surgery

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Introduction

For a significant period of time, breast conservation treatment (BCT) has been considered to provide similar survival outcomes as mastectomy for the treatment of breast cancer (McLaughlin, 2013). However, a recent study suggests that BCT may be associated with a higher breast cancer specific survival rated than mastectomy or mastectomy with radiation (Agarwal et al., 2014). In the light of this new data, one could consider BCT as the preferred modality of surgical treatment for breast cancer when eligibility criteria are fulfilled. In Western countries, BCT rates are often reported to be in excess of 60% (Table 1) (Lee et al., 2009; McGuire et al., 2009; Garcia-Etienne et al., 2012; Agarwal et al., 2014). This is in contrast to Asian communities where the average reported rates of BCT are considerably lower (Table 1) (Chuwa et al., 2009; Yau et al., 2009; Yip et al., 2009; Chang et al., 2011; Jung et al., 2011; Wang et al., 2011; Gadgil et al., 2012). The discrepancy in BCT rates between Western and Asian communities have been commonly attributed to physical, socio-cultural and surgeon factors (Woon and Chan, 2005; Dixon and Mak, 2008; Yau et al., 2009; Rippy et al., 2014). It is known that Asian women tend to have smaller breast tissue volume than their western counterparts, (Qiao et al., 1998; Yau et al., 2009) and some authors consider women with smaller volume breast tissue to be poor candidates for BCT (Kronowitz et al., 2006). These arguments might lead to a conclusion that Asian women have a lower eligibility for BCT. This study was undertaken to evaluate the validity of this syllogism, and if utilisation of BCT in Asian women can be improved. If possible, higher rates of breast conservation could lead to better survival outcomes in Asian women (Agarwal et al., 2014).

Materials and Methods

A retrospective analysis of all patients with breast malignancies who underwent operative treatment by a single surgeon at a private medical facility between 2009 and 2011 was performed. Preoperative percutaneous needle biopsies were done for diagnosis where possible. If there was insufficient compression thickness or discordant imaging and biopsy results, the patient underwent a surgical diagnostic procedure.

Following diagnosis, patients deemed eligible for BCT were given the option of an attempt at breast conservation or mastectomy, with or without reconstruction. Eligibility

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for BCT was made based on the surgeon's assessment of the ability to achieve a reasonable cosmetic result after tumour resection with clear margins. If the tumour was assessed to be too large, the patient was offered neoadjuvant medical therapy, and had placement of radio-opaque clip(s) prior to its commencement. These were localised before wide excision, which was guided by the position(s) of the marker clip(s).

Patients who elected for an attempt at BCT underwent surgery with intraoperative frozen section analysis for margin status to lower re-excision rates. Successful BCT was defined by pathologic clear margins and completion of all recommended adjuvant treatment. Breast conservation was performed solely using local tissue rearrangement or volume displacement techniques, with none having volume replacement with flaps or implants.

Statistical analyses were performed using SPSS (Chicago, IL) version 11 advanced statistical software module. Comparisons of categorical variables were performed using the chi-squared test where appropriate. Continuous variables with median or mean values were compared using the Mann- Whitney U test.

Results

A total of 163 patients underwent surgical treatment during the study period. Two patients were excluded as they did not complete the recommended adjuvant treatment, leaving 161 patients for analysis. Demographic features, clinicopathologic characteristics and surgical procedures performed for the study population are presented in Table 2. One hundred and sixteen (72%) had palpable tumours while 45 (28%) patients presented with screen detected lesions. One hundred and thirty-eight patients (85.7%) received BCT. Of the 138 women who underwent BCT, 95 (68.8%) had symptomatic lesions while 43 (31.2%) had screen detected lesions. Twenty-three patients underwent mastectomy. Fifteen (65.2%) of these twenty-three were performed based on necessity as recommended by the surgeon.

The reasons for mastectomy included large non-invasive tumour, poor response to neoadjuvant chemotherapy with insufficient downstaging, inadvertently missed multicentric tumour and diffuse indeterminate calcifications for which patient could not tolerate MRI surveillance. The patient with the inadvertently missed multicentric tumour presented with a palpable lesion at the 2 o'clock position of the left breast. This was associated with a large area of microcalcifications. Initial bracketing and wide excision of this lesion demonstrated a 55 mm ductal carcinoma in situ (DCIS) with clear margins. However, the postoperative mammogram following the initial attempt at breast conservation demonstrated another area of microcalcifications at the 12 o'clock position of the ipsilateral breast. It was concluded that the multicentric focus of disease was not detected at first because of the superimposition of calcifications on imaging. She subsequently underwent a completion left mastectomy. Histology demonstrated a further 15 mm DCIS at the superior aspect of the breast.

Eight patients elected to undergo a mastectomy

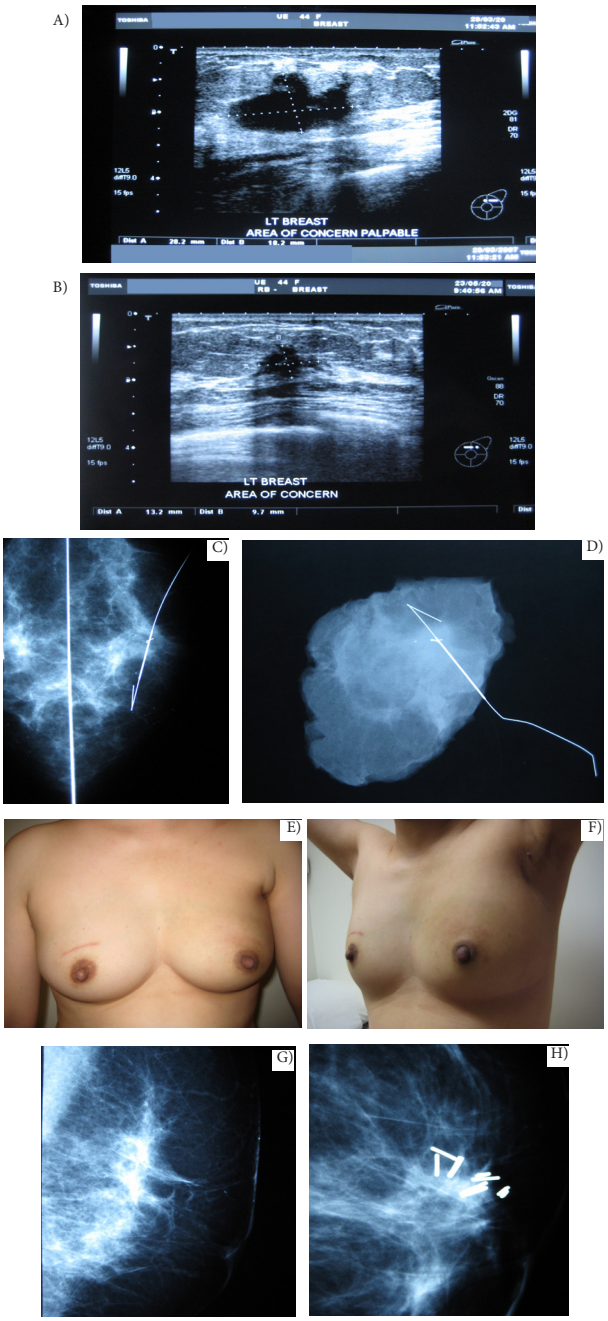

Figure 1. A-H Standard Approach for a Typical Chinese Patient with Smaller Breast Tissue Volume (B-cup), Presenting with a Tumour Assessed to be Too Large for Successful Breast Conservation Treatment (BCT) at the Time of Diagnosis. Neoadjuvant chemotherapy reduced this invasive ductal carcinoma of the left breast from an imaging size of 28 mm to 13 mm. A wide excision was performed based on the localised radio-opaque clip originally positioned at the time of core biopsy. Residual 3 mm invasive disease was noted at pathology with clear margins. No residual disease was found in the lymph nodes after left axillary dissection, although a positive cytology was returned prior to induction chemotherapy. The final cosmetic outcome is shown in Figures E & F, two years after completion of treatment. The incision on the right breast was for the excision of a benign lesion at the request of the patient. She is currently disease-free. The incision directly over the tumour bed facilitates radiotherapy and negates the need for multiple clips placed to demarcate the original tumour site. Figure G shows this patient's most recent mammogram, in comparison with Figure 1H, one from another patient who had BCT elsewhere

despite the surgeon's recommendation for BCT. The reasons given by these patients included a preference for avoidance of radiotherapy, patient's perception of superiority of mastectomy despite evidence otherwise and the incorrect assumption that a mastectomy would preclude the necessity of chemotherapy. The patient who held this last opinion developed regional recurrence nine months after her mastectomy, and was finally persuaded to undergo chemotherapy. She remains well 44 months after repeat excision and chemotherapy.

There were 23 patients who had invasive tumours too large for BCT at the time of presentation, and all underwent primary medical therapy for tumour downstaging. Fourteen of these had sufficient tumour shrinkage for successful BCT. Nine patients underwent mastectomy, amongst whom one elected to have a mastectomy despite being a suitable candidate for conservation. Where tumour size at presentation was assessed to be too large, 60.9% had adequate downstaging for successful BCT. Figures 1A-G illustrates the usual outcome for such a clinical scenario.

In general, patients underwent the surgical procedure recommended by the surgeon. However, there were 8 patients who elected to undergo a mastectomy in favour of an attempt at BCT (5.4%). The mean tumour size of these 8 patients was 18.8mm (SD 13.7mm) compared with a mean tumour size of 19.7mm (SD 12.3mm) for all patients with BCT (p=0.83). It would therefore reasonable to predict that successful BCT would have been possible had these patients decided to proceed with breast conservation surgery as recommended, making eligibility for BCT 146 of 161 (90.7%) and utilisation 138 of 146 (94.5%). The mean tumour size of those who underwent mastectomy as recommended was 40.5mm (SD 25.3mm). This was significantly larger than tumour size for BCT (p=0.013). In addition, the mean age for women who elected to undergo mastectomy was significantly higher than those who had BCT (56.6 vs 48.6 years, p=0.037).

Table 1 lists a summary of reported BCT rates from various regions of the world. While the dominant ethnic group of this study population was Chinese, a fair proportion were Caucasian and of other Asian origins. The latter group of women included Malays, Indonesians, Indians, Bangladeshis, Eurasians, Vietnamese, Myanmese and Japanese. There was no significant difference in BCT rates amongst the different ethnic groups, and it would be reasonable to conclude that Asian women have equivalent eligibility for BCT compared with their Western counterparts. The data also suggests that ethnicity does not act as a bias against BCT.

The median follow up period for this study cohort is 44 months. So far, there one patient with mastectomy (4.3%) had a local recurrence at 7 months after surgery. This patient presented with a 10 cm tumour 8 months after diagnosis at another centre. During neoadjuvant chemotherapy, she developed signs of inflammatory breast cancer and was referred for mastectomy due to disease progression. She was noted to have brain metastasis shortly after and died 15 months after her surgery. Two patients with BCT (1.2%) developed local recurrence. The first patient presented with a 40 mm metaplastic carcinoma of the right breast and underwent BCT after a partial response following neoadjuvant treatment. Recurrence was detected four months after surgery, and she had a mastectomy. She is currently well 52 months after her second procedure. The second patient developed a recurrence 26 months after BCT. She is unfortunately lost to follow-up. These events are summarised in Table 2. In addition to the patient who had a recurrence seven months after a mastectomy discussed earlier, another patient who underwent mastectomy developed distant disease and succumbed 56 months after treatment. Two women who underwent BCT developed metastatic disease without local recurrence at 12 months and 22 months after

Table 1. Comparison of Published Data for BCT Rates

Author	Centre/Country/Study Period	n	Characteristics	% BCT
International/Western				
Agarwal et al., 2014	SEER database (1998-2008)	132 149	Tumour ≤4 cm, ≤3 lymph node +	70%
McGuire et al., 2009	Moffitt Cancer Centre, FL, USA (1994-2007)	5865	Stage 0-IV	63.70%
Lee et al., 2009	University of Michigan Medical Centre, Michigan, USA (2003-2005)	993	Tis-T4	63%
Garcia-Etienne et al, 2012	EUSOMA (2003-2010)	15,369	Stages 0, I, II (stage III,T3/T4 excluded)	73.30%
Local				
Chuwa et al., 2009	National Cancer Centre Singapore (2002-2003)	767	Symptomatic	28.20%
			Screen detected	45.20%
			Stage 0-IV	31.50%
Wang et al., 2011	Changi General Hospital, Singapore (2002-2008)	761	Symptomatic	18.50%
			Screen detected	40.20%
			Stage 0-IV	23.30%
Chang et al., 2011	National University Hospital, Singapore (1990-2007)	2449	Stage 0-IV	29.20%
Woon and Chan, 2005	Tan Tock Seng Hospital, Singapore (2000-2002)	389	Stage I,IIB (T1-T2)	39.10%
Regional (South Asia/East Asia)				
Yip et al., 2009	University of Malaya Medical Centre (2001-2005)	953	T1,T2	29.70%
Yau et al., 2009	Pamela Y. Nethersole Eastern Hospital, Hong Kong (1994-2007)	2375	T1,T2	30%
Gadgil et al., 2012	Bhabha Atomic Research Centre Hospital, Mumbai (2005-2010)	99	T1-T4	42.20%
Jung et al., 2011	Korean Breast Cancer Society database (2008)	13,908	Stage 0,I	58%
Current Study	MammoCare, Singapore (2009-2011)	116	Symptomatic	81.80%
		45	Screen detected	95.60%
		161	Stage 0-IV	85.70%

*BCT: Breast conservation treatment; SEER: Surveillance, Epidemiology and End-Result; FL: Florida, USA: United States of America

Table 2. Summary of Demographic, Clinicopathologic and Outcome Data for Study Population

Clinicopathologic characteristic		All patients (n=161) (%)	BCT(n=138) (%)	Mastectomy (n=23) By need (%)	Mastectomy (n=23) By choice (%)	p value
Age in years	Median (Range)	48 (28-78)				
	Mean (SD)	48.8 (9.8)	48.3 (10)	50.1 (8.8)		0.48
	Mean (SD)		48.3 (10)		56.50(5.6)	**0.004**
Ethnicity	Chinese	106 (65.8)	91/106 (85.8)	8/106 (7.5)	7/106 (6.6)	0.87
	Malay/Indonesian	11 (6.8)	9/11 (81.8)	2/11 (18.8)		
	Indian	12 (7.5)	11/12 (91.7)	1/12 (8.3)		
	Other Asian	14 (8.7)	13/14 (92.9)	1/14 (7.1)		
	Caucasian	18 (11.2)	14/18 (77.8)	3/18 (16.7)	1/18 (5.5)	
Mode of Presentation	Symptomatic tumours	116 (72.0)	95/116 (81.9)	13/116 (11.2)	8 (6.9)	**0.02**
	Screen detected lesions	45 (28.0)	43/45 (95.6)	2/45 (4.4)	0	
	All patients	161	138/161 (85.7)	15/161 (9.3)	8/161 (5.0)	
Tumour size in mm (range)	Median (Range)	19.0 (4-97)	19.7 (12.4)	40.5 (28.0)		**0.012**
	Mean (SD)	21.6	19.7 (12.4)		18.8(13.7)	0.85
T	1	100 (62.1)	92/100 (92.0)	4/100 (4.0)	4/100 (4.0)	
	2	50 (31.1)	39/50 (78.0)	7/50 (14.0)	4/50 (8.0)	
	3	8 (5.0)	5/8 (62.5)	3/8 (37.5)	0	
	4	3 (1.8)	2/3 (66.7)	1/3 (33.3)		
Stage at diagnosis	0	20 (12.4)	18/20 (90.0)	1/20 (5.0)	1 (5.0)	**<0.001**
	I	67 (41.6)	66/67 (98.5)	1/67 (1.5)	0	
	II	55 (34.2)	46/55 (83.6)	4/55 (7.3)	5/55 (9.1)	
	III	18 (11.2)	8/18 (44.4)	8/18 (44.4)	2/18 (11.1)	
	IV	1 (0.6)	0	1		
Histological Type	DCIS	20 (12.4)	18/20 (90.0)	1/20 (5.0)	1/20 (5.0)	0.39
	Invasive Ductal	125 (77.6)	108/125 (86.4)	11/125 (8.8)	6/125 (4.8)	
	Invasive Lobular	7 (4.4)	5/7 (71.4)	1/7 (1.4)	1/7 (1.4)	
	Other invasive	9 (5.6)	7/9 (77.8)	2/9 (22.2)		
Grade	DCIS	20 (12.4)	18/20 (90.0)	1/20 (5.0)	1/20 (5.0)	0.54
	1	28 (17.4)	27/28 (96.4)	1/28 (3.6)	0	
	2	59 (36.6)	49/59 (83.0)	6/59 (10.2)	4/59 (6.8)	
	3	50 (31.1)	40/50 (80.0)	7/50 (14.0)	3/50 (6.0)	
	Unknown	4 (2.5)	4/4 (100.0)			
Neoadjuvant medical therapy	Yes	23 (14.3)	14/23 (60.8)	8/23 (34.8)	1/8 (12.5)	**<0.001**
	No	138 (85.7)	124/138 (89.8)	7/138 (5.1)	7/138 (5.1)	
Disease Extent	Unifocal	121 (75.2)	104/121 (86.0)	11/121 (9.1)	6/121 (4.9)	0.06
	Multiple foci at diagnosis	40 (24.8)	34/40 (85.0)	4/40 (10.0)	2/40 (5.0)	
Recurrence	Local Recurrence	3 (1.9)	2/138 (1.4)	11/121	0/8	0.08
	Distant Disease/Death	4 (2.5)	2/138 (1.4)	4/40	0/8	
Median Follow-up (months) (range 18-63)		44				

*BCT: breast conservation surgery; SD: standard deviation

surgery. The first died at 14 months and the second at 30 months after treatment, giving a mortality of 1.4% of the patient cohort with BCT. In total, after a median follow up of 44 months, 2.5% of the study group has died from breast cancer.

Discussion

For about three decades, BCT and mastectomy have been considered to provide equivalent survival for women with breast cancer (McLaughlin, 2013). There is now recent data to suggest that BCT may confer a higher breast cancer-specific survival rate compared with mastectomy (Agarwal et al., 2014). Although the reasons behind this observation have yet to be clearly elucidated, this new information elevates the role of BCT in women with early breast cancer. Thus, a low rate of BCT, as seen in Asian populations, may not offer optimum survival.

Most series of surgical treatment of breast cancer in Asian countries report BCT rates lower than 55%. Table 1 lists BCT rates from different regions. It has been postulated that the BCT rates in Asia could be attributable to cultural unpopularity of the procedure and small breast tissue volume (Yau et al., 2009). However, in this series, when given the opportunity to make an informed choice, only 8 patients of the projected eligible 148 patients (5.4%) elected to have mastectomy over an attempt at BCT. The data suggests that given the choice, the majority of Asian women may prefer BCT. In fact, there was no significant difference in BCT rates amongst the various ethnic groups in the study cohort. The majority of the patients in the study cohort were Chinese, and expected to have similar physical attributes in terms of breast tissue volume as Chinese women elsewhere. Still, BCT rates in the study cohort are higher than in other Chinese-dominant countries (Chuwa et al., 2009; Yau et al., 2009; Yip et al., 2009; Chang et al., 2011; Wang et al., 2011) and are similar to, if not also higher than, those reported in Western countries (Lee et al., 2009; McGuire et al., 2009; Garcia-Etienne et al., 2012; Agarwal et al., 2014). Hence, the issue of smaller breast tissue volume and its impact on BCT rates needs further investigation.

Surgeon preferences and manner of communicating recommendations have been considered a significant factor in influencing patients' decision-making processes and eventual choice of surgery (Woon and Chan, 2005; Dixon and Mak, 2008; Rippy et al., 2014). Data from the current study supports these theories. More than 90% of women agreed to undergo the surgical procedure recommended by the surgeon and just 5.4% opted for

a different operation. A mastectomy was recommended only when tumour size was assessed to be too large for BCT. In this study, the mean tumour size of the patients who were recommended mastectomy was significantly larger than for those who underwent BCT.(40.5mm vs 19.7mm, p=0.012) There was no significant difference in tumour sizes for women who underwent BCT and those who elected for mastectomy despite being assessed to be suitable candidates for conservation. (19.7mm vs 18.8mm, p=0.85) If this last group of patients had undergone successful BCT, the BCT rate in this cohort could have been 90.8%. Based on the final pathologic size of the tumour, it appears that the preoperative assessment of successful BCT is consistent regardless of patient's choice.

Those choosing a mastectomy against surgeon's recommendations were older than those in the BCT group, suggesting that age is a contributing factor in patient's choice for type of surgical procedure. This is different from data in a western community where there was no age trend. In fact, 23.4% of women aged 50 years or younger chose a mastectomy, while 17.3% of women older than 50 years chose a mastectomy over BCT (McGuire et al., 2009).

Women with smaller volume breast tissue, as is the tendency in Asian communities, (Qiao et al., 1997; Yau et al., 2009) are thought to be poor candidates for BCT using local tissue rearrangement techniques (Kronowitz et al., 2006). Hence, when performing BCT for such women, the use of volume replacement is recommended by some in anticipation of poor aesthetic results (Kronowitz et al., 2006; Nahabedian et al., 2013). The use of volume replacement approaches with flaps and implants are associated with higher complication rates (Israeli et al., 2014) than volume displacement procedures with parenchymal closure (Kronowitz et al., 2006, Indelicato et al., 2007). The latter approach should therefore be the technical procedure of choice (Kronowitz et al., 2006). For women with smaller volume breast tissue, there are manoeuvres that can be applied to achieve higher BCT rates, (Tan, 2007; 2009; 2010; 2012) which in turn offer potential for better survival outcomes (Agarwal et al., 2014).

There is controversy regarding the use of preoperative MRI in women who are newly diagnosed with breast cancer. In order to increase BCT rates, the authors prefer a selective approach on the use of MRI (Tan, 2009) as its routine use increases the odds of having a mastectomy without significant reduction in re-excision rates or mortality (Houssami et al., 2013). Without MRI, there might be occasions when ipsilateral synchronous tumours are missed. These are extremely rare occurrences and it is the authors' opinion that the low possibility does not warrant a policy of routine preoperative MRI. However, further investigations may be needed to aid in the process of selecting appropriate candidates for MRI, and one such indication could be diffuse bilateral calcifications.

The impact of tumour biology on loco-regional recurrence was dealt with in a recent review (Morrow, 2013). The concept that certain tumour types would be better served by a mastectomy in terms of local control was shown to be unfounded, and pathologic type is not a factor for consideration in selecting candidates for BCT (Morrow, 2013). Therefore, tumour size and the surgeon's clinical assessment of adequate retained parenchymal volume following wide excision to allow tissue rearrangement for a reasonable cosmetic outcome forms the sole basis for estimation of successful BCT.

Mastectomy not only leads to an inferior long term psychological outcome, (Sun et al., 2013) it also results in poorer quality of life which is perceived to be worse than an amputation (Akkaya et al., 2011). In an effort to overcome this, a considerable proportion of patients wish for immediate breast reconstruction following mastectomy to 'feel whole again' (Shameen et al., 2008). BCT avoids the need for reconstruction, provides for better long-term psychological outcome and avoids the negative impact on body image. Furthermore, there is now evidence that BCT confers improved breast cancer- specific survival (Agarwal et al., 2014). For best outcomes for patients with breast cancer, steps should therefore be taken to modify factors associated with higher mastectomy rates (Roder et al., 2013). It is encouraging that active measures are being made in certain countries to increase BCT rates (Omranipour et al., 2014) despite the current trend of rising trend of mastectomy in others (McGuire et al., 2009).

In this small series of patients, it has been shown that BCT using only local tissue rearrangement techniques is a viable option for Asian women. The small size of the cohort is one of the limitations of this study. Also, the study population comes from patients who underwent treatment in a private hospital setting, representing a group of better educated women from higher socio-economic backgrounds and may not be entirely reflective of the general population. Nevertheless, it does offer data indicating that higher BCT rates than currently reported in Asian countries is possible, potentially leading to better breast cancer –specific survival (Agarwal et al., 2014).

In conclusion, in this study, 85.7% cohort underwent BCT for the treatment of breast cancer. It was anticipated that 146 of 161 patients (90.7%) were eligible for BCT. Since 8 women declined BCT, the uptake of BCT was 94.5%, or 138 of a possible 146. Of women with presenting with palpable tumours, 82.3% had successful BCT and among those with screen detected lesions, 95.6% had BCT. These rates are not inferior to those reported in Western communities. The reasons for lower BCT rates in previous series reported from Asian countries are not immediately clear. It is however, anticipated that patient education, clinician motivation and the application of appropriate surgical techniques may contribute to increased BCT rates. Recent data suggests that we stand on the threshold of a new era of breast cancer surgery, where BCT offers superior rather than equivalent survival outcomes (Agarwal et al., 2014). It is therefore timely that data from this study serves as a basis for further research in these areas to improve utilisation of BCT among Asian women.

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