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Patient-reported outcome measures among breast cancer survivors: A cross-sectional comparison between Malaysia and high-income countries

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Abstract

Objectives: Patient-reported outcomes (PROs) in high-income countries (HICs) suggest that physical, emotional, and psychological needs are important in cancer care. To date, there have been few inconsistent descriptions of PROs in low-income and middle-income Asian countries. Using a standard questionnaire developed by the International Consortium for Health Outcomes Measurement (ICHOM), we compared the perceived importance of PROs between patients in Malaysia and those in HICs and between clusters of Malaysian women.

Methods: Breast cancer patients were recruited from three Malaysian hospitals between June and November 2017. We compared the proportion of patients who rated PROs as very important (scored 7-9 on a 9-point Likert scale) between Malaysian patients and data collected from patients in HICs via the ICHOM questionnaire development process, using logistic regression. A two-step cluster analysis explored differences in PROs among Malaysian patients.

Results: The most important PROs for both cohorts were survival, overall well-being, and physical functioning. Compared with HIC patients (n = 1177), Malaysian patients (n = 969) were less likely to rate emotional (78% vs 90%), cognitive (76% vs 84%), social (72% vs 81%), and sexual (30% vs 56%) functioning as very important outcomes ($P < 0.001$). Cluster analysis suggests that older, parous, Malaysian women, who were less likely to have received breast reconstructive surgery, were more likely to rate body image and satisfaction with the breast as very important outcomes.

Conclusion: Taking into account the differences in PROs by cultural and socioeconomic settings could improve patient expectation of services and refine the assessment of cancer care outcomes.

KEYWORDS

Asian, breast cancer, cancer, LMIC, oncology, patient-reported outcomes, quality of life, survivor

1 | INTRODUCTION

In Asia, the number of new breast cancers cases are expected to rise by more than 40% by 2030[1] because of changes in lifestyle and reproductive risk factors.[2,3] Efforts are underway to improve treatment options and access to quality cancer care among women living in Asia, and as such, the pool of breast cancer survivors with unmet needs continues to grow.

Patient reported outcomes (PROs) refers to any response that is collected directly from patients using various methods and instruments.[4] Cross-sectional studies in predominantly high-income countries (HICs) have shown that emotional and psychological well-being are common themes among breast cancer survivors.[5-9] These studies also found that the main needs after diagnosis or treatment are management of long-term side effects as well as physical, cognitive, and sexual functioning needs,[5,6,10] while longitudinal studies highlight that fear and feelings of uncertainty evolve over time after diagnosis.[11-14]

A limited number of studies on patient outcomes among minority groups in developed countries indicate that ethnic and regional differences exist.[11,14] Interestingly, a study of American breast cancer survivors revealed that African-American women reported higher psychosocial and sexual functioning compared with White women.[15] In a study comparing breast cancer patients from Germany and Hong Kong, both HICs with comparable standards of breast cancer care, Hong Kong Chinese women were less likely to report unmet psychosocial, sexual, physical, and daily living needs but were more likely to express needs in health service delivery.[16]

Given that the majority of the research on PROs has been conducted in developed or HICs, it is important to understand the differences or similarities in how women in low and middle income countries (LMICs) interpret their cancer care priorities.[17,18] In LMICs, the differences in socioeconomic status,[19] health literacy,[20] the condition of the healthcare system, and various mitigating factors could deeply influence the perceptions and outcomes for breast cancer survivors. Therefore, we hypothesize that breast cancer survivors' priorities will differ between LMICs and HICs, as well as within populations.

In this study, we sought to compare the perceived importance of PROs among breast cancer patients from Malaysia, a middle-income country, to the outcomes of patients from HICs, using the patient-centered outcomes questionnaire for breast cancer recently

TABLE 1 Distribution of breast cancer patients by demographic and clinical features

Characteristics	Distribution of Malaysian Patients (n = 969)	
	n	%
Age (mean = 54.5 ± 10.6)		
Race		
Chinese	714	73.7
Malay	172	17.8
Indian	72	7.4
Others	10	1.0
Education level		
None	15	15.5
Primary	114	11.8
Secondary	381	39.3
College and University	446	46.0
Married	798	82.4
Number of children (mean = 2.1 ± 1.5)		
Nulliparous	209	21.6
Recruitment site		
SJMC	405	41.8
ParkCity	183	18.9
UMMC	330	34.1
Others	51	5.3
Questionnaire administered by		
Patient	287	29.6
Research assistants	660	68.1
Language used		
English	498	51.4
Chinese dialects	330	34.1
Malay	141	14.6
Stage at first diagnosis		
0	70	7.2
1	299	30.9
2	326	33.6
3	169	17.4
4	26	2.7
Recurrence reported	30	3.1

Abbreviations: SJMC, Subang Jaya Medical Centre; UMMC, University of Malaya Medical Centre.

TABLE 2 Differences in demographic and clinical features between Malaysians and HIC patients

Characteristics	Malaysian Patients (n = 969)		HIC Patients (n = 1177)		*P* value
	n	%	n	%	
Age					
<45 y	190	19.6	125	10.6	**<0.001**
46-65 y	630	65.0	885	75.2	
>65 y	148	15.3	162	13.8	
Duration after diagnosis					
<2 y	331	34.2	82	7.0	**<0.001**
2-10 y	550	56.8	930	79.0	
>10 y	87	9.0	165	14.0	
Metastatic disease	34	3.5	91	7.7	**<0.001**
Currently on treatment	577	59.6	510	43.3	**<0.001**
Treatment received					
Surgical treatment					
Mastectomy	571	58.9	632	53.7	**0.015**
Lumpectomy	390	40.3	514	43.7	0.110
Breast reconstruction	106	10.9	296	25.1	**<0.001**
Non-surgical treatment					
Chemotherapy	564	58.2	760	64.6	**0.003**
Radiotherapy	634	65.4	753	64.0	0.484
Hormone therapy	623	64.3	798	67.8	0.087
Targeted therapy	82	8.5	173	14.7	**<0.001**

Includes both past and current treatment.

developed by the International Consortium of Health Outcomes Measurement (ICHOM). We also sought to explore the differences in perceived importance of PROs within different clusters of Malaysian women.

2 | METHODS

2.1 | Questionnaire

We used a standard suite of value-based, patient-centered outcomes questionnaire for breast cancer developed by ICHOM in 2016. Briefly, the questionnaire was developed through a working group of clinicians, nurses, epidemiologists, breast cancer survivors, and advocacy groups and involved structured literature reviews and focus group discussions.[21] Outcomes that were voted by at least 70% of the working group were included in the questionnaire, using a modified two-round Delphi approach. The final questionnaire included four outcome domains, namely, survival and disease control, quality of life and functioning, symptoms, and disutility of care. The PROs in each domain is measured on a Likert scale of 1 (not important) to 9 (extremely important). In this cross-sectional study, the questionnaire was translated into local Malaysian languages.

2.2 | Participants

All incident and prevalent breast cancer survivors (n = 1063) were recruited between June and November 2017 from three outpatient clinics and at cancer-related events in suburban areas of the Klang Valley, in Malaysia. Women were approached to participate if they were Malaysian and if they had a confirmed history of breast cancer diagnosis within the past 15 years. Patients' particulars and demographics were collected with written, informed consent. During the same visit, the ICHOM survey was either self-administered or administered by research assistants. Questionnaires with ≥50% missing responses (n = 16), missing date of first diagnosis (n = 3), repeat questionnaires (n = 13), questionnaires without signed consent forms (n = 42), and ineligible women (20) were excluded from analyses. The final analysis was conducted on 969 women.

As part of the validation process in the development of the ICHOM questionnaire, 1225 patients from international patient organizations in Europe (51%), Australia (41%), and North America (7%)

TABLE 3 Comparison of patient reported outcome measures ratings between Malaysian patients (n = 969) and HIC patients (n = 1177)

Patient Reported Outcome Measures	Malaysian Patients			HIC Patients			Malaysian vs HIC Patients Adjusted analysis[a]	
	Median score	Rated 7-9		Median score	Rated 7-9			
		n	%		n	%	Odds ratio (95% CI) [b]	*P* value
Survival and disease control								
Overall survival	9	832	85.9	9	1119	95.1	0.33 (0.21-0.51)	**<0.001**
Recurrence free survival	9	876	90.4	9	1117	94.9	0.51 (0.30-0.88)	**0.014**
Quality of life and functioning								
Overall well-being	9	887	91.5	9	1035	87.9	1.24 (0.87-1.78)	0.238
Physical functioning	9	859	88.6	8	1058	89.9	0.82 (0.58-1.14)	0.236
Emotional functioning	8	759	78.3	8	1060	90.1	0.42 (0.31-0.55)	**<0.001**
Cognitive functioning	8	735	75.9	8	993	84.4	0.62 (0.48-0.80)	**<0.001**
Ability to work	8	757	78.1	8	971	82.5	0.81 (0.63-1.04)	0.096
Social functioning	8	694	71.6	8	946	80.4	0.68 (0.54-0.86)	**0.001**
Body image	7	549	56.7	7	748	63.6	0.89 (0.73-1.09)	0.891
Sexual functioning	5	291	30.0	7	662	56.2	0.35 (0.28-0.44)	**<0.001**
Satisfaction with breast	6	449	46.3	7	627	53.3	0.88 (0.71-1.08)	0.877
Anxiety	7	488	50.4	6	526	44.7	1.27 (1.04-1.55)	**0.021**
Depression	7	472	48.7	6	498	42.3	1.26 (1.02-1.54)	**0.029**
Symptoms								
Fatigue	6	447	46.1	7	702	60.1	0.60 (0.49-0.73)	**<0.001**
Arthralgia	6	450	46.4	7	581	49.4	0.90 (0.73-1.10)	0.307
Vasomotor symptoms	5	293	30.2	6	530	45.0	0.60 (0.48-0.74)	**<0.001**
Peripheral neuropathy	6	435	44.9	6	498	42.3	1.12 (0.91-1.37)	0.295
Pain	7	480	49.5	6	458	38.9	1.63 (1.33-2.00)	**<0.001**
Breast symptoms	7	496	51.2	6	413	35.1	1.95 (1.59-2.39)	**<0.001**
Vaginal symptoms	5	350	36.1	5	366	31.1	1.43 (1.15-1.77)	**0.001**
Disutility of care								
Major complications	8	579	59.8	7	516	43.8	1.74 (1.40-2.15)	**<0.001**

[a]All models were adjusted for age, duration since diagnosis, incidence of metastatic disease, current treatment, and past treatment,

[b]95% Confidence interval

anonymously responded to the ICHOM survey.[22] Using the same set of exclusion criteria as for Malaysian women, we analyzed the data for 1177 women from HICs.

2.3 | Statistical analysis

Comparison of data between Malaysian patients and HIC patients were done using Pearson chi-square tests. Multivariable logistic regressions were used to compare the likelihood of rating an outcome as very important (rating 7-9 on the Likert scale) between Malaysian patients and HIC patients, adjusting for potential confounding variables, namely, age, duration since diagnosis, incidence of metastatic disease, current treatment, and past treatment.

We conducted a two-step cluster analysis among Malaysian patients. In the clustering step, we included age, ethnicity, education, marital status, parity, recruitment site, questionnaire administration, and history of mastectomy and breast reconstructive surgery. Our final model consisted of three clusters with fair cluster quality and with least missing data (13%). We compared the proportion that rated the PROs as very important (rated 7-9 on the Likert scale) across the three clusters, using Pearson chi-square tests.

All hypothesis tests were two sided, and P value < 0.05 was considered as statistically significant. SPSS Software [version 21] was used for all data analysis.

3 | RESULTS

In this cross-sectional study, most of the Malaysian participants were recruited from private hospitals (60.7%) and were of Chinese ethnicity (73.7%, Table 1). About two-thirds of the participants were diagnosed with early stage breast cancer (American Joint Committee on Cancer (AJCC) Stage 1 and 2, 71.7%) and are currently on treatment (59.6%).

3.1 | Comparison between Malaysian and HIC patients

Compared with patients from HICs (n = 1177), the Malaysian participants were less likely to be diagnosed more than 10 years ago, (9.0% vs 14.0% among HIC patients, P < 0.001), with fewer cases of metastatic disease (3.5% vs 7.7%, P < 0.001, Table 2). There were more Malaysian patients under 45 years old (19.6% vs 10.6%, P < 0.001). More Malaysian participants were still undergoing treatment at the time of the interview (59.6% vs 43.3%, P < 0.001). Although Malaysians had more mastectomies than patients from HICs (58.9% vs 53.7%, P = 0.015), fewer Malaysians had undergone breast reconstruction (10.9% vs 25.1%, P < 0.001).

In Table 3, we show the most important outcomes for Malaysian women include overall well-being (91.5% rated as very important), recurrence free survival (90.4%), physical functioning (88.7%), and overall survival (85.9%). Vasomotor symptoms (30%), sexual functioning (30%), and vaginal symptoms (36%) were least commonly rated as very important. It is notable that 9% of patients were unable to respond to the questions about the latter two outcomes (Table S1). The most important outcomes for HIC patients were similar to that for Malaysian patients.

Malaysian patients were less likely than HIC patients to rate emotional (78% vs 90%), cognitive (76% vs 84%), social (72% vs 81%), and sexual (30% vs 56%) functioning as very important outcomes (P < 0.001). Interestingly, marginally more Malaysian patients rated anxiety (50% vs 45%, P = 0.021) and depression (49% vs 42%, P = 0.029) as very important outcomes.

Fatigue and arthralgia were of less concern to Malaysian patients (46% vs 60% and 30% vs 45%, respectively, P < 0.001). Malaysians were also less likely to rate vasomotor symptoms as a very important outcome (30% vs 45%, P < 0.001). However, more Malaysian women rated pain (50% vs 39%) and breast symptoms (51% vs 35%) as very important outcomes, compared with patients from HICs (P < 0.001).

3.2 | Cluster analysis among Malaysian patients

From the two-step cluster analysis, three distinct clusters emerged (Table S2). Clusters 1 and 2 consisted of married, parous women (n = 184 and n = 479, respectively). Women in cluster 1 were younger (mean age = 52), were more likely to be Chinese (91.8%), and had some tertiary education (62%). Fewer women in cluster 2 had undergone breast reconstruction (8.6%) compared with patients in cluster

TABLE 4 Cluster analysis of Malaysian women

Patient Reported Outcome Measures	Cluster 1 (n = 184)		Cluster 2 (n = 479)		Cluster 3 (n = 181)		*P* value
	n	%	n	%	n	%	
Survival and disease control							
Overall survival	152	82.6	418	87.3	152	84.0	0.115
Recurrence free survival	152	82.6	446	93.1	167	92.3	0.569
Quality of life and functioning							
Overall well-being	149	81.0	461	96.2	170	93.9	**<0.001**
Physical functioning	138	75.0	450	93.9	164	90.6	**<0.001**
Emotional functioning	123	66.8	398	83.1	147	81.2	**<0.001**
Cognitive functioning	117	63.6	382	79.7	140	77.3	**<0.001**
Ability to work	124	67.4	389	81.2	149	82.3	**<0.001**
Social functioning	109	59.2	363	75.8	131	72.4	**<0.001**
Body image	78	42.4	306	63.9	96	53.0	**<0.001**
Sexual functioning	46	25.0	157	32.8	42	23.2	**0.036**
Satisfaction with breast	68	37.0	243	50.7	82	45.3	**0.011**
Anxiety	84	45.7	243	50.7	102	56.4	0.175
Depression	80	43.5	230	48.0	102	56.4	0.061
Symptoms							
Fatigue	69	37.5	233	48.6	87	48.1	**0.033**
Arthralgia	79	42.9	235	49.1	78	43.1	0.271
Vasomotor symptoms	49	26.6	148	30.9	55	30.4	0.596
Peripheral neuropathy	69	37.5	231	48.2	73	40.3	**0.030**
Pain	69	37.5	248	51.8	99	54.7	**0.002**
Breast symptoms	88	47.8	240	50.1	98	54.1	0.401
Vaginal symptoms	56	30.4	192	40.1	56	30.9	**0.030**
Disutility of care							
Major complications	88	37.5	310	64.7	106	58.6	**0.001**

1 (16.8%). Cluster 3 consisted of unmarried, nulliparous women (n = 181) and was similar to cluster 1 in age and educational profile. The women in cluster 1 were less likely to have been administered the survey by research assistants (14.7%) compared with cluster 2 (93.5%) and cluster 3 (70.7%).

When comparing PROs across the three clusters in Table 4, there were no significant differences between the clusters in the rating of survival and disease control outcomes. Interestingly, the older, married women in cluster 2 were more likely than the younger clusters to rate body image (63.9% vs 42.4% and 53.0% for clusters 1 and 3, respectively, $P < 0.001$), satisfaction with the breast (50.7% vs 37.0% and 45.3%, $P = 0.011$), and vaginal symptoms (40.1% vs 30.4% and 30.9%, $P = 0.030$) as very important. Pain was a more important outcome for the younger, unmarried women in cluster 3 (54.7%) compared with clusters 1 and 2 (37.5% and 51.8% respectively, $P = 0.002$). Also, patients in cluster 3 appear to be more concerned with anxiety and depression, but the differences were not statistically significant. We also found that surveys administered by research assistants were significantly more likely to yield a 7 to 9 rating for many of the PROs, compared with self-administered surveys, but there were significant independent effects for age, ethnicity, education, and/or marital status in post hoc multivariable regression analysis (Figure S1).

4 | CONCLUSIONS

4.1 | Discussion

In this cross-sectional study, we found that survival and disease control, overall well-being, and physical functioning remain the most important PROs for both Malaysians and HIC patients. However, compared with HIC patients, Malaysians were less likely to rate emotional, cognitive, social, and sexual functioning as very important and were more likely to prioritize symptoms and complications management. We also found that among Malaysian women, age, ethnicity, education, and parity may influence perceived importance of PROs.

We found that survival, well-being, and physical functioning were the primary outcomes of importance in this study, for both the Malaysian and HIC patients. This is consistent with many longitudinal, cross-sectional, and qualitative studies that have been conducted.[6,8,9,22,23] A review of such studies revealed that breast cancer recurrence and fear of death are common themes among patients newly diagnosed with breast cancer and often manifest early and persist over time.[10] Therefore, the prioritization of getting healthy and remaining healthy is likely consistent across populations. However, the ways in which these needs are met may be different across economic and racial groups.[11,14] Therefore, population-specific physician-patient communication tools and effective educational materials may assist in important decision making processes within targeted groups.[10]

Our study shows that fewer Malaysians view sexual functioning as very important. This is consistent with a 2011 study where German women were more likely than their Asian comparators to report sexuality as an unmet need.[16] Open expressions or discussions about sexuality are still a deeply ingrained taboo in most parts of Asia.[24-26] This conservatism among Asian women is further reflected in the relatively high proportion of women who chose not to rate the questions about sexuality in the Malaysian cohort, almost 10%. Therefore, the low importance subscribed to sexuality in this study of Asian women may be a reflection of the difficulties faced by women in communicating their sexual needs to their medical care providers.

Interestingly, while body image and satisfaction with the breast appearance were not prioritized among Asian women in general, we found a cluster of older, married women Asian women who were more likely to report these outcomes as very important. This is in contrast to other studies that found that body image and sexuality are important issues primarily among younger breast cancer survivors.[27] While cultural conservatism about sexuality is one aspect of this difference,[24,28,29] the greater emphasis on body image could be ascribed to the significantly fewer breast reconstructive surgeries in this group[30] and may represent difficulties faced by women in coping with these issues after mastectomy. Further analysis on how to support women in making decisions about mastectomy and reconstructive surgery may be helpful in Asian populations.

We found that Asian women were less likely to view emotional functioning as very important, compared with women in HICs. However, the Asian women in our study were marginally more likely that their HIC counterparts to rate anxiety and depression as very important. Studies have observed that Asians are more likely to downplay psychological issues that remain plagued with taboo.[31,32] In this group of urban, well-educated Asian women, however, the higher perceived importance of anxiety and depression may be directly associated with an increased awareness of mental health issues and the general lack of access to mental health care in the region. In LMICs, only 0.5% of the health budget is spent on mental health, compared with an average of 5.1% in HICs.[33] Addressing the mental health needs of Asian women, in parallel to their breast cancer treatment, remains a critical area for improvement.

4.2 | Clinical implications

To the best of our knowledge, this is the first study to quantitatively describe PROs for breast cancer survivors in a middle-income country. The strength of this study lies in the relatively large sample size of multiethnic Asian women from whom we collected data using a standardized survey developed and validated among patients in HICs, which enabled effective comparisons between the two populations. This is a crucial element to improving service delivery in this region and could enable cross-cultural adoption of effective interventions to increase quality of life among breast cancer survivors across diverse population settings.

This study also adds to our currently limited understanding about PROs or breast cancer survivor priorities in Malaysia. The few studies conducted in Malaysia have been small in size and have utilized various assessment tools that prevent the identification of subgroups that may have different priorities in their cancer care.[34-38] From our study, we hypothesize that a woman's age, marital status, education history, and ethnicity drive what she perceives to be important in her care

after a breast cancer diagnosis. This information can enable the health care team to better understand and cater to the needs of diverse Malaysian breast cancer survivors.

4.3 | Limitations

There were several limitations to the study. Firstly, this study involved interviews with patients diagnosed up to 15 years ago, which makes it prone to recall biases. The differences in how the survey was administered could have led to some biases (including sampling bias) in the findings. We were not able to account for some factors that could have influenced perception, such as financial status. Also, the questionnaire did not undergo a process of validation for this population prior to its use and therefore, may be less reliable than desired. For the Malaysian cohort, the results may not truly represent the Malaysian population as the patients were recruited from hospitals serving urban areas in two Malaysian states. Only 20% of Malaysian breast cancer survivors in our study were diagnosed at late stage (Stage 3 and 4), compared with the national average of 49%.[39] Therefore, we may not have captured the priorities for patients with more severe disease.

4.4 | Conclusion

We show significant differences in perceived importance of PROs between breast cancer survivors in an Asian middle-income country compared with predominantly Caucasian HICs, and that population-specific research is crucial to better clinician-patient relationship, patient care, and satisfaction and assess the outcomes of cancer care.

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CONFLICT OF INTEREST

The authors listed in this manuscript have no conflict of interests to declare.

ETHICAL APPROVAL

This study adheres to the principles outlined in the Declaration of Helsinki and was approved by the Independent Ethics Committee Ramsay Sime Darby Health Care [Ref: 201704.1] and the University of Malaya Research Ethics Committee (UMREC) [Ref: 201745-5122].

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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