RESEARCH ARTICLE

Development and Evaluation of a Patient-Reported Outcome (PRO) Scale for Breast Cancer

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Abstract

Background: This study was guided by principles of the theoretical system of evidence-based medicine. In particular, when searching for evidence of breast cancer, a measuring scale is an instrument for evaluating curative effects in accordance with the laws and characteristics of medicine and exploring the establishment of a system for medically assessing curative effects. At present, there exist few tools for evaluating curative effects. Patient-reported outcomes (PROs) refer to outcomes directly reported by patients (without input or explanations from doctors or other intermediaries) with respect to all aspects of their health. Data obtained from PROs provide evidence of treatment effects. Materials and Methods: In accordance with the tenets of theoretical medicine and ancient medical theory regarding breast cancer, principles for developing a PRO scale were established, and a theoretical model was developed and a literature review was performed, items from this pool were combined and split, and an initial scale was constructed. After a pilot survey and additional modifications, a pre-questionnaire scale was formed and used in a field investigation. After the application of statistical methods, the item pool was used to create a formal scale. The reliability, validity and feasibility of this formal scale were then assessed. Results: In a clinical investigation, 479 responses were recovered, with an acceptance rate of 95%. a combination of various methods was employed, and the items that were selected by all methods or more than half of the methods were employed in the questionnaire. In these cases, the screening methods were combined with certain features of the item, A total of four domains and 38 items were reserved. The reliability analysis indicated that the PRO scale was relatively reliable. Conclusions: Scientific assessment proved that the proposed scale exhibited good reliability and validity. This scale was readily accepted and could be used to assess the curative effects of medical therapy. However, given the limited scope of this investigation, the capacity for adapting this scale to incorporate other theories could not be determined.

Keywords: PRO scale - breast cancer - evaluation of clinical curative effect

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Introduction

Patient-reported outcomes (PROs) comprise a recently proposed evaluation system of therapeutic efficacy that is based on the subjective feelings of patients. A PRO directly reflects patients' perspectives on various aspects of their health statuses Data obtained by PRO measurements provide evidence for therapeutic efficacy from the perspectives of patient. PRO includes the functional status or objective symptom indices and health-related quality of life. PRO also includes a patient's satisfaction towards treatment. PRO equally emphasizes the quality-of-life index, the objective symptom index and the non-entity index. Using this knowledge as a guide and modern mathematical statistics as a tool, this study preliminarily established a PRO scale for evaluating breast cancer after surgery (Zhao et al., 2005; Cella et al., 2007; FDA., 2007; Pusic et al., 2009; Arbuckle et al., 2010; Pusic et al., 2013)

The molecular typing-based, individualized precision therapy for breast cancer warrants a good survival rate for breast cancer. A large number of breast cancer patients achieve postoperative long-term survival or manage to survive in the presence of tumours. However, the vast majority of patients experience a variety of health, psychological and behavioural problems related to the disease. Patients suffer not only the general psychological burden of malignant tumours but also the immense psychological impact caused by loss of a breast. The inclusion of PROs in the evaluation of clinical treatment not only compensates for the current lack of indices for evaluating the clinical efficacy of breast cancer treatment but also allows a patient's condition to be assessed more

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accurately than would be possible with universally applicable scales without PROs. (Pusic et al., 2009; Kanatas et al., 2012; Ohsum et al., 2013; Pusic et al., 2013)

Internationally, the quality-of-life scales that are extensively employed for breast cancer have served an important role in guiding our research. This study represents a bold attempt and innovation. Application of the PRO scale in the evaluation of the clinical efficacy of individualized breast cancer therapy is the direction of our research.

Materials and Methods

Generation of primary questionnaire and implementation of clinical survey

Using the established method of formulating PRO scale as reference, a group composed of breast cancer patients, medical experts and statistical experts was set up, and an envisioned conceptual structural model of a breast cancer-specific PRO scale was established. The model had a five-dimensional structure that consisted of five domains, including physiology, psychology, independence, social relations and the environment.

Selection of items of the PRO scale

The methods that were employed to coarsely screen the items included item difficulty analysis and response analysis. The items were re-screened using the following methods: Dispersion tendency analysis and stepwise regression analysis. In the pre-survey, the total score given by patients to their quality of life represents the total situation of the quality of life of patients. Factor analysis and cluster analysis were used to select items based on representativeness. Discriminant analysis-this method primarily selects items from the aspect of distinguishability. Cronbach's coefficient-this method primarily selects items from the aspect of internal consistency. In this study, the items were classified and examined based on the theoretical structure that was used to design the scale.

Scientific assessment of the PRO scale

A scientific assessment of the feasibility, reliability and validity of the PRO scale was conducted. The scientific assessment was completed using the SPSS 15 statistical software package. During the assessment of the structural validity of the scale, the confirmatory factor analysis, the

Table 1. The Preliminary Version of the Breast Cancer-Specific PRO Questionnaire

1. Pain at surgical site	21. Nausea and heartburn	41. Dependence on drugs
2. Discomfort and numbness at surgery site	22. Dryness and bitterness in the mouth	42. Adoption of anticancer diet
3. Skin itching and dryness in surgical area	23. Abdominal bloating and pain	43. Impact of disease on daily life
4. Upper arm movement disorder on the side of surgery	24. Constipation	44. Impact of disease on marriage
5. Numbness and pain in the upper arm on the side of surgery	25. Diarrhea	45. Impact of falling ill at work
6. Upper arm swelling on the side of surgery	26. Hair loss	46. Living an energetic life
7. Distension and pain in contralateral breast	27. Hot flushes and sweats	47. Confidence to overcome disease
8. Lump in contralateral breast	28. Increased sensitivity to cold	48. Support from friends and family
9. Lump in armpit	29. Insomnia	49. Closeness to spouse
10. Menoxenia	30. Sad and negative feelings	50. Degree of satisfaction with sexual life
11. Abnormal vaginal discharge	31. Bad mood	51. Degree of satisfaction with transportation to hospital
12. Pain in the joints of the extremities	32. Easily angers and loses temper	52. Quality of medical service
13. Dizziness and tinnitus	33. Easily experiences irritability and anxiety	53. Degree of satisfaction with therapeutic efficacy
14. Soreness and weakness in the waist	34. Frequently feels nervous due to the disease	54 Degree of satisfaction with the attending physician
15. Dry eyes	35. View of personal illness	55. Quality of life
16. Heart palpitations	36. Side effects of treatment	
17. Chest tightness and pain	37 Fear of metastasis	
18. Shortness of breath	38. Fear of disease progression	
19. Cough and expectoration	39. Fear of infection	
20. Decreased appetite	40 Fear of long-lasting discomfort	

affiliate software of SPSS 15.0-AMOS 7-was employed. The feasibility assessment included the clinical usage of the breast cancer-specific PRO scale and the time required to complete the scale. The reliability assessment adopted two common methods: Cronbach's α coefficient and split-half reliability. The validity of the PRO scale was primarily evaluated from three aspects: content, structure and distinguishability. Assessments of construct validity included an exploratory factor analysis and a confirmatory factor analysis (Anthoine et al., 2014; Fiscella et al., 2011; Luquiens et al., 2015; Mills et al., 2010; McAllister et al., 2011).

Results

Generation of the preliminary version of the PRO questionnaire

Patients who satisfied the diagnostic criteria for breast cancer, already underwent surgery, were capable of expressing their opinions and had no mental illness were included. The patients were interviewed from different aspects and appropriately guided. The information was collected and summarized into items. A clinical survey was conducted using the preliminary questionnaire in the breast surgery clinics of three major hospitals. A total of 200 patients were interviewed. A total of 67 questionnaire items was generated; this number was revised by breast surgery experts. After these revisions, 55 items were included in the preliminary version of the

Table 2. General Information About the Samples

	Patients	Number	Percentage
Age	20<n≤35	24	5
	35<n≤50	189	39.5
	50<n≤70	243	50.7
	n>70	23	4.8
Marrige	Married	357	74.5
	Unmarried	122	25.5
Breastfeeding	Already	324	67.6
	No	155	32.4
Economic conditions	Very good	25	5.2
	Good	107	22.3
	General	302	63
	Poor	45	9.4
Course of disease	≤1 year	139	29
	1<n≤2	104	21.7
	2<n≤3	158	33
	3<n≤5	78	16.3

Table 3. The Results of Various Screening Approaches for Assessing the Breast Cancer-Specific PRO Questionnaire

Items	Dispersion tendency	Stepwise regression	Factor analysis	Cluster analysis	Discriminant analysis	Cronbach's coefficient	Selected items
1. Pain at the surgical site	#		#	#		#	*
2. Discomfort and numbness at the surgical site	#		#	#	#	#	*
3. Skin itching and dryness in the surgical area	#	#	#	#	#	#	*
4. Upper arm movement disorder on the ipsilateral side	#		#		#	#	*
5. Numbness and pain in the upper arm on the ipsilateral side	#		#		#	#	*
6. Upper arm swelling on the ipsilateral side	#		#	#		#	*
7. Distension and pain in the contralateral breast	#	#	#	#	#	#	*
8. Lump in the contralateral breast	#		#		#		
9. Lump in an armpit	#		#	#	#		*
10. Menoxenia	#		#	#	#		*
11. Abnormal vaginal discharge	#			#	#	#	*
12. Pain in the joints of the extremities	#		#	#	#		*
13. Dizziness and tinnitus	#		#	#	#	#	*
14. Soreness and weakness in the waist	#	#	#	#	#	#	*
15. Dry eyes	#		#	#	#	#	*
16. Heart palpitations	#		#		#	#	*
17. Chest tightness and pain	#		#	#	#	#	*
18. Shortness of breath			#		#	#	
19. Cough and expectoration	#				#	#	
20. Decreased appetite			#	#		#	

Items	Dispersion tendency	Stepwise regression	Factor analysis	Cluster analysis	Discriminant analysis	Cronbach's coefficient	Selected items
21. Nausea and heartburn			#			#	
22. Dryness and bitterness in the mouth	#			#	#	#	*
23. Abdominal bloating and pain			#	#	#	#	*
24. Constipation	#		#	#			
25. Diarrhoea			#			#	
26. Hair loss	#		#	#			
27. Hot flushes and sweats	#		#	#		#	*
28. Increased sensitivity to cold	#		#	#		#	*
29. Insomnia	#		#	#	#	#	*
30. Sad and negative feelings	#		#	#	#	#	*
31. Bad mood			#		#	#	
32. Easily becomes angry and loses temper	#		#	#		#	*
33. Easily experiences irritability and anxiety	#		#		#	#	*
34. Frequently feels nervous due to the disease	#	#	#		#	#	*
35. View of personal illness	#		#		#	#	*
36. Side effects of treatment	#	#	#	#	#	#	*
37 Fear of metastasis	#		#	#		#	*
38. Fear of disease progression	#		#			#	
39. Fear of infection	#		#			#	
40 Fear of long-lasting discomfort	#		#			#	
41. Dependence on drugs	#		#	#		#	*
42. Adoption of an anticancer diet	#			#	#	#	*
43. Impact of disease on daily life	#		#		#		
44. Impact of disease on marriage					#	#	
45. Impact of falling ill at work	#		#	#		#	*
46. Living an energetic life	#		#		#	#	*
47. Confidence to overcome disease			#		#	#	
48. Support from friends and family						#	
49. Closeness to spouse		#	#		#	#	*
50. Degree of satisfaction with sexual life	#		#		#		
51. Degree of satisfaction with transportation to the hospital	#	#	#		#	#	*
52. Quality of medical service	#		#		#	#	*
53. Degree of satisfaction with therapeutic efficacy	#	#	#	#	#	#	*
54 Degree of satisfaction with the attending physician	#	#	#		#	#	*
55. Quality of life							*

PRO questionnaire (Table 1).

These items of the proposed scale were divided into the following five domains: physiology, psychology, personal life, social relations and social environment.

General information about the samples

A total of 479 female outpatients were examined. The majority of patients (51.6%) ranged between 35 and 50 years of age. The distribution of the course of disease

Table 4. The Final Breast Cancer-specific PRO Questionnaire

Items	items
1. Pain at the surgical site	20. Increased sensitivity to cold
2. Discomfort and numbness at the surgical site	21. Insomnia
3. Skin itching and dryness in the surgical area	22. Sad and negative feelings
4. Upper arm movement disorder on the ipsilateral side	23. Easily becomes angry and loses temper
5. Numbness and pain in the upper arm on the ipsilateral side	24. Easily experiences irritability and anxiety
6. Upper arm swelling on the ipsilateral side	25. Frequently feels nervous due to the disease
7. Distension and pain in the contralateral breast	26. View of personal illness
8. Lump in an armpit	27. Side effects of treatment
9. Menoxenia	28. Fear of metastasis
10. Abnormal vaginal discharge	29. Dependence on drugs
11. Pain in the joints of the extremities	30. Adoption of an anticancer diet
12. Dizziness and tinnitus	31. Impact of falling ill at work
13. Soreness and weakness in the waist	32. Living an energetic life
14. Dry eyes	33. Degree of satisfaction with sexual life
15. Heart palpitations	34.Degree of satisfaction with transportation to the hospital
16. Chest tightness and pain	35. Quality of medical service
17. Dryness and bitterness in the mouth	36. Degree of satisfaction with therapeutic efficacy
18. Abdominal bloating and pain	37. Degree of satisfaction with the attending physician
19. Hot flushes and sweats	Total quality-of-life score

Table 5. The Structure of the Final Version of the Breast Cancer-specific PRO Scale

Domains	Aspects	Items
Medical treatment	Common symptoms after breast cancer surgery	1-6, 9
	Common side effects of radiochemotherapy and endocrine therapy	10-12, 16, 19, 27, 17
Medical theory	Physiological manifestation of tumour	7, 8
	Subhealth conditions	13-15, 18, 20,21
Scale theory and medical psychology	Positive aspects	30, 32
	Negative aspects	22-25, 27,28, 29
	Neutral questions	26, 31, 33
Degree of satisfaction towards treatment environment	Satisfaction with treatment environment	34-37

considerably varied (Table 2).

Results of various screening methods and the final structure of the breast cancer-specific PRO scale

In the process of reviewing and screening the items, the items selected by different methods were not completely identical. Therefore, a combination of various methods was employed, and the items that were selected by all methods or more than half of the methods were employed in the questionnaire. Some items cannot be determined by these methods. In these cases, the screening methods were combined with certain features of the item, such as professional knowledge and operability, and scale reliability and validity assessment to determine whether the item should be included or excluded. A total of four domains and 37 items were reserved. In addition, a self-evaluation item regarding the quality of life was added. Therefore, a total of 38 items were included in the questionnaire (Tables 3 and 4). The structure of the final version of the breast cancer-specific PRO scale is presented below (Table 5).

Based on the structure, the score of a domain/aspect of the scale was the cumulative score of the items that belonged to the domain/aspect. A grading system was set up to classify the items in the PRO scale into five grades. The five grades had scores of one, two, three, four or five points, where one point denoted the worst grade and five points denoted the best grade. High scores indicate a high quality of life, whereas low scores indicate a low quality of life. However, various domains contained different numbers of items, which hindered the comparison between the scores of the domains. Therefore, the average score of each domain was calculated, which enabled a comparison between the domains.

Assessment of the reliability and validity of the PRO scale

The results of the reliability assessment showed that the breast cancer-specific PRO scale exhibited good reliability. The results also indicated that the related syndrome elements only experienced a low degree of disturbance in the process of utilizing the scales to summarize the pathogenesis of breast cancer, which may clarify the main symptom of the clinical syndrom. The validity results showed that the first factor included items that reflected information in four domains: psychology, independence, social relationships and social environment. Therefore, we believe that the PRO scale possessed not only construct validity but also content validity. Therefore, the study findings indicated that the current PRO scale exhibited satisfactory discriminant validity .

Discussion

PRO measures not only evaluate the efficacy of a stage of treatment but also serve a certain guiding role in the next stage of treatment. Based on the screening results, the items that we proposed to address complications were reserved; this finding was consistent with clinical situations. Regarding the side effects of radiochemotherapy and endocrine therapy, items including gastrointestinal reactions and hair loss were removed based on the screening results. The medical cases selected for this study involved patients who received surgery more than six months ago, these symptoms have minimal effects on the total health of the patients. Items reserved in the final version of the PRO scale addressed the side effects, including the side effects of endocrine therapy, drug-induced osteoporosis, and toxic reactions of the cardiovascular system induced by Adriamycin and other chemotherapy drugs. These side effects are long-lasting and have a significant impact on the health of the patients.

The results showed that the majority of the deleted items were derived from FACT-B. Most patients gave more attention to subjective feelings of symptoms instead of the quality of life when completing the questionnaire. According to the patients, the discomfort symptoms caused additional suffering. The results are consistent with our expectations. A PRO emphasizes subjective feelings. The focus of PRO differs from the focus of the quality of life scales and readily reflects the significance of developing PROs. The items in the PRO scale that belong to the domains of social relations and environment were also screened. The results showed that the items that address marriage, sexual life and emotions should be deleted. We believe that many patients do not provide accurate real answers due to pride or other reasons. Therefore, we should protect patients' rights of privacy in future studies. Therefore, the scale failed to successfully evaluate the long-term therapeutic efficacy. In addition, the scale was unable to reflect dynamic changes over time. We will continue to enrich the content and improve the construction of the PRO scale to obtain better evaluations of therapeutic efficacy.

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