Original Article

Mapping functions of cancer patients' quality of life in Indonesia: from EORTC-QlQ -C-30 to EQ-5D-5L

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ABSTRACT

The instruments for measuring cancer patients' quality of life are available for many cancer types, but none of them are showing a utility score. It is important to map the functions of the specific instruments into the generic instrument to get the utility score. This study is aimed to define the mapping of functions in the Indonesian version of EORTC QLQ C-30 into the Indonesian version of EQ-5D-5L. We collected data and QoL from 469 patients in some hospitals in central Java and Sumatera, Indonesia. The inclusion criteria were adult cancer patients who were treated with chemotherapy. Patients were excluded if had comorbidities, complications, or were pregnant and during lactation. We performed OLS regression for getting the mapping. Our subjects were dominated by females, with advanced stages of cancer and between 25-59 yo (69.4%; 54.1%; 86%, respectively). The global health score of EORTC QLQ C-30 is lower than the VAS of EQ-5D-5L. The most symptom experienced is pain. We got two models for mapping functions of the questionnaire, and model 2 had better performance with lower values of MAE and RMSE. Model 2 involves physical, role, and emotional functions, pain, dyspnea, insomnia, and financial difficulties as the variable which can be mapped into EQ-5D-5L. Our study found that some functions in EORTC QLQ C-30 had a significant correlation with EQ 5D 5L domains. These results can be used to get the utility value of Indonesian cancer patients, and they can be applied to define the cost-utility of the targeted drug for cancer.

Keywords: Mapping, Cancer, EORTC QLQ C-30, EQ 5D, Indonesia, Utility

Introduction

Cancer is still becoming a burden in Indonesia. The new cases of cancer in Indonesia were 396.914 from 270 million people. The number of death reached 234.511 and the prevalence cases for 5 years reached 946.088 [1]. The cost of cancer treatment in Indonesia reached $486,960,633 in 2016 [2]. Most of the cancer cases were other cancers, including breast cancer, followed by cervix, lung, and colorectal cancer. The high burden of cancer in Indonesia can be seen from the productivity impact loss of earnings in Indonesia, as much as IDR 23,174 trillion in 2018 [3]. Currently, Food and Drug Administration (FDA) already approved some targeted therapies which presented the success of treatment in some types of cancer [4]. However, not every country can include the targeted therapies in the National Health Insurance system, due to the expensive price [5]. Thus, we need the pharmacoeconomic analysis to consider the benefit, utility, and effectiveness of the targeted therapies compared to the cost of the drug [6].

For defining the utility index, which will be used in the pharmacoeconomic formulations, the appropriate instruments must be used, for instance, the EQ-5D-5L, which is available in Indonesia set value [7]. Another instrument which consisted of the general domain of quality of life also can be applied [5]. The generic questionnaire does not represent the condition of cancer patients, which experience some effects due to disease or the side effect of chemotherapy. EORTC-QLQ-C30 is one of the quality-

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Perwitasari DA, Candradewi SF, Purba FD, Septiantoro BP. Mapping functions of cancer patients' quality of life in Indonesia: from EORTC-QlQ -C-30 to EQ-5D-5L. J Adv Pharm Educ Res. 2023;13(3):19-22. https://doi.org/10.51847/avg60W3aR5

of-life questionnaires which is most frequently applied in cancer patients. This questionnaire is also available in Bahasa Indonesia [8]. Unfortunately, this questionnaire does not present the utility value, thus, we need to do the mapping functions between EORTC-QLQ-C30 and EQ-5D-5L to define the utility index.

This study has an objective to define the mapping of functions in the Indonesia version of EORTC QLQ C-30 into the Indonesian version of EQ-5D-5L

Materials and Methods

We conducted a cross-sectional study in some public hospitals located in central Java and Sumatera from 2019-2020. We recruited 469 cancer patients with inclusion criteria: adult cancer patients, under the treatment of chemotherapy, with only one participation during their cycles. Patients were excluded if had comorbidities, complications, or were pregnant and during lactation. We proceeded the inform consent to the subjects before the recruitment process. This study has been approved by the Hospital Ethic Committee number: Number: .401/EC/KEPK-RSDK/2019.

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) was used as the disease-specific questionnaire. EORC-QLQ-C30 consists of five functions, such as; physical, emotional, social, role, cognitive, three symptom scales (fatigue, nausea, vomiting, pain), and six items for various symptoms, such as shortness of breath, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties. Additionally, one general health status scale is also measured [8].

The EQ-5D-5L was used as a generic quality-of-life instrument. The EQ-5D-5L has been proven to be valid and reliable to be used on the Indonesian population [7]. This questionnaire consists of two parts: the descriptive system and the EQ-visual analog scale (EQ-VAS). This questionnaire consisted of five dimensions such as mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of the domains can take one of five severity level responses (no problems, slight problems, moderate problems, severe problems, and unable/extreme problems). The EQ Visual Analogue Scale (EQ-VAS) presents the respondent's self-rated health on a 20 cm vertical visual analog scale with endpoints labeled "the best health you can imagine" and "the worst health you can imagine".

We performed Ordinary Least Square regression for getting the utility mapping of EORTC-QLQ-C30 and EQ-5D-5L.

Results and Discussion

We recruited 469 cancer patients from three public hospitals. Most of the patients were female (69.9%), they were adults (86.6%), mostly in the advanced stage of cancer (55.4%), and covered by national health insurance (98.1%). **Table 1** present the patient characteristics in the three hospitals).

Table 1. Patients' characteristics

Characteristic	Number of patients (N=469)	Percentage (%)
Sex		
Men	141	30.1
Women	328	69.9
Age		
Adult	406	86.6
Women	63	13.4
Cancer Stadium		
Early stage	85	18.1
End-stage	260	55.4
No information	124	26.4
Insurance		
BPJS	460	98.1
Private	124	1.9
Last Education		
No Education	20	4.3
Elementary School	146	31.1
Junior High School	67	14.3
Senior High School	141	30.1
Undergraduate	91	19.4
No Information	4	9
Work		
Yes	180	38.4
No	289	61.6
Salary per month (IDR)		
> 2.500.000	262	42.9
< 2.500.000	201	42.85
No information	6	1.3
Marital Status		
Married	411	87.6
Not married	58	12.4

Table 2 describes the score of the questionnaires' domains. The highest score of EORTC QLQ-C-30 is a better quality of life. The highest score is cognitive function and the lowest score is role function (89.27 and 65.99, respectively). The worst symptoms of EORTC-QLQ-C30 can be seen from the highest score of the symptoms, thus fatigue is the worst symptom experienced by cancer patients in this study (39.35). In general, the quality of life of cancer patients is not good, because the global health score only reaches 68.66. The utility index reaches 0.68, which presents a similar value to the global health of EPRTCQLQ-C30. The visual analog scale rates 72.58.

Table 3 presents the results of ordinary least square regression, which shows the MAE and RMSE. The MAE and RMSE of model 3 are smaller than those of model 1.

Table 4 describes in detail the comparison of the two models, seeing the domains which can influence the model.

Table 2. Utility and domain scores (n=469)

EQ5D5L	Mean	SD
Utility	0.65	0.37
Visual Analog Scale	72.58	14.61
EORTC QLQ C30		
Functions		
Physical	73.94	**26.07**
Role	65.99	**33.94**
Emotional	83.06	**19.62**
Cognitive	89.43	**15.99**
Social	80.96	**23.99**

Symptoms		
Weakness	**39.35**	**25.30**
Nausea-Vomiting	**25.27**	**26.42**
Pain	**35.68**	**37.89**
Dyspnea	**6.97**	**19.58**
Insomnia	**34.19**	**36.97**
Loss of Appetite	**32.84**	**32.71**
Constipation	**15.92**	**27.60**
Diarrhea	**7.25**	**18.73**
Financial difficulties	**32.12**	**34.32**
General QoL	**68.66**	**20.62**

Table 3. Results of OLS (N = 469)

Model	Mean Actual (SD)	Mean Predicted (SD)	Mean Absolute Error (SD)	Adjusted R-Square	RMSE
Model 1: Full	0.65395 (0.327341)	0.65353 (0.326996)	0.17987 (0.13169)	0.758	0.2228
Model 2: Backward	0.65396 (0.325729)	0.65337 (0.326185)	0.13951 (0.12894)	0.756	0.1898

Table 4. Comparison of the models

	Model 1			Model 2		
	β	**S.E**	***p-value***	**β**	**S.E**	***p-value***
Intercept	-0.170	0.106	0.109	-0.096	0.057	0.091
Physical function	0.008	0.001	0.000	0.008	0.000	0.000
Role function	0.001	0.000	0.019	0.001	0.000	0.001
Emotional function	0.001	0.001	0.000	0.002	0.000	0.000
Cognitive function	0.000	0.001	0.562			
Social function	0.000	0.000	0.698			
Weakness	-0.001	0.000	0.092			
Nausea-vomiting	0.000	0.000	0.441			
Pain	-0.001	0.000	0.000	-0.001	0.000	0.000
Dyspnea	-0.001	0.000	0.004	-0.002	0.000	0.000
Insomnia	-0.001	0.000	0.037	-0.001	0.000	0.002
Loss of appetite	-0.005	0.000	0.814			
Constipation	0.000	0.000	0.253			
Diarrhea	0.000	0.000	0.808			
Financial difficulties	-0.001	0.000	0.001	-0.001	0.000	0.001
Quality of life	0.001	0.000	0.011			
Sex	0.019	0.019	0.319			
Age	0.005	0.026	0.854			

Our study defines that physical, role, and emotional functions, pain, dyspnea, insomnia, and financial difficulties, have a significant impact on the utility score of cancer patients in Indonesia. This model is important to get the utility value of cancer patients in Indonesia, which will be used in the pharmacoeconomic analysis of the targeted therapies. Currently, the available utility score in Indonesia is based on the general population condition and measured using EQ-5D-5L [7]. However, cancer patients have complicated situations, which can influence their quality of life. The disease effect and the treatment itself may deteriorate their quality of life [9]. Another consideration of measuring the patients' quality of life is the subjective perception of the patients towards their health and well-being [10, 11]. Thus, using the appropriate instrument for measuring their quality of life is very important [12].

The quality of life of cancer patients in our study is not good. Fatigue is the most complained symptom which may influence physical function. Due to the limitation of physical function, the role of cancer patients in doing a daily activities is also limited. Thus, the score of the role function is low. The previous meta-analysis shows that the worst function in cancer patients was emotional function, however, the other functions had a score above 70. This meta-analysis also presented that fatigue and financial difficulties are the most common symptoms experienced by cancer patients [13]. A previous study also mentioned that only 20% of the cancer patients had a good quality of life, and the rest had moderate and poor quality of life [14]. Our study results are also inline with previous study in colorectal cancer, which mentioned that, the good quality of life can be seen in all functions, with the lowest score is emotional function [15]. In a particular country, the quality of life showed a high score, it can be caused by the infrastructure for early detection of cancer, patients' education and pre-treatment for minimizing the side effect of cancer treatment [13, 16, 17].

In the model of mapping functions, pain also has a significant influence on the utility score. Our study is in line with the previous study which mentioned that pain is significantly associated with distress and interferes with the daily life of cancer patients.

The cancer patients complained the moderate to severe intensity of pain during the cancer treatment [18]. The previous study about mapping functions of EORTC-QLQ-C30, EQ-5D-5L, and FACT -G, shows that the EQ-5D-5L index can be generated from the EORTC-QLQ-C30 and FACT-G. However, there are some limitations in that the model cannot be applied in the very good health conditions of the two instruments and the poor health of the FACT-G [19].

Another previous study, conducted in many countries, concluded that the mapping of EORTC QLQ-C30 into EQ-5D-3L, the role function, and loss of appetite did not have a significant influence in predicting the EQ-5D. The study presented many models which can be used based on the level of quality of life of the cancer patients [20].

Our study has a limitation because we did not conduct the sub-group analysis based on the level of patients' quality of life. However, to the date of our knowledge, this topic is the first one conducted in Indonesia, thus the result will be assisting the decision-making body to perform the pharmacoeconomic analysis, especially in considering the

Conclusion

The EQ-5D-5L can be generated from EORTC-QLQ-C30, to define the utility score in pharmacoeconomic analysis. The significant functions and symptoms which may interfere with

cancer patients' quality of life are physical, role, emotional functions and pain, dyspnea, insomnia, and financial difficulties the symptoms.

Acknowledgments: Ministry of Research and Technology/ Badan Riset dan Inovasi Nasional No: 9/E1/KPT/2021 for the research grant.

Conflict of interest: None

Financial support: Ministry of Research and Technology/ Badan Riset dan Inovasi Nasional No: 9/E1/KPT/2021 for the research grant.

Ethics statement: This study has been approved by the Hospital Ethic Committee number: Number: .401/EC/KEPK-RSDK/2019.

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