

## RESEARCH ARTICLE

# Evaluation of Health-Related Quality of Life among Patients with Cervical Cancer in Indonesia

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### Abstract

**Background:** Evaluation of health-related quality of life (HRQOL) in cervical cancer patients is important in order to design the interventions for improving patient outcomes. Reports of HRQOL among cervical cancer patients in Indonesia are limited. Moreover, measurement using EQ-5D-3L is to our best knowledge has hitherto not been performed. This study aimed to examine the HRQOL of cervical cancer patients in Indonesia using EQ-5D-3L. **Materials and Methods:** A cross-sectional study was conducted by interviewing cervical cancer patients using the EQ-5D-3L questionnaire. Percentages of patients who reported having problems in each dimension of EQ-5D as well as EQ-5D index score (utility) were calculated. **Results:** Our findings indicated that the most frequent reported problems were pain/discomfort (67.8%) followed by anxiety/depression (57.5%). The mean of EQ-5D VAS was 75.8 (SD=17.0). The mean (SD) utility scores were 0.85 (0.19), 0.76 (0.20), 0.71 (0.21), and 0.77 (0.13) for cervical cancer patients in stage I, II, III, and IV, respectively. **Conclusions:** Cervical cancer significantly affects patient HRQOL. Efforts should be made to improve the quality of life of cervical cancer patients especially in terms of pain /discomfort and anxiety/depression reduction.

**Keywords:** Cervical cancer -EuroQol-5D (EQ-5D) - quality of life - utility - Indonesia

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### Introduction

The global burden of cervical cancer is high with the majority of the cases occurred in developing countries. Cervical cancer is the third most prevalent cancer in the world. In South-East Asian region, it is the second most prevalent cancer after breast cancer (Moore et al., 2010; Ferlay et al., 2012). The partial cancer registry in Indonesia reported the same trend that cervical cancer is the second most common cancer among women (Wahidin et al., 2012). In Indonesia, the incidence and mortality rate of cervical cancer are 17 per 100,000 populations and 7.7 per 100,000 populations, respectively (Ferlay et al., 2012). The strategies for prevention and control of cervical cancer include the modalities of primary prevention strategies (vaccination program), secondary prevention strategies (screening), and tertiary prevention strategies (treatment with standard-of-care). The implementation of those strategies might differ between settings. Hence, the modalities should be selected for the most appropriate for the local conditions and patients (Karimi Zarchi et al., 2009; Reeler et al., 2009).

Both disease and its treatment have negative impact

on quality of life of cervical cancer patients. In disease like cancer, patients are no longer focus only on how long they live but also health related quality of life (HRQOL). Evaluation of HRQOL in cervical cancer patient is important in order to design the intervention for improving patients' outcome as well as to monitor and evaluate the effectiveness of treatment and intervention. HRQOL measures include comprehensive aspect of the disease and treatment impacts in terms of symptoms, therapeutic effects, side effects, patient functional status, and financial impact (Higginson and Carr, 2001; Grzankowski and Carney, 2011). Two types of instrument could be used to measure HRQOL in cancer patient, namely specific instrument and generic instrument (Teckle et al., 2011). The examples of specific instrument that can be used for measuring HRQOL in cervical cancer patients are the European Organization for the Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire Core 30 (QLQ-C30) (Aaronson et al., 1993) and Quality-of-Life questionnaire cervical cancer module (QLQ-CX24) (Greimel et al., 2006), the Functional Assessment of Cancer Therapy-General (FACT-G) (Cella et al., 2010), and Functional Living Index-Cancer (FLIC) (Schipper et al.,

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1984). The examples of generic instrument for measuring HRQOL are the EuroQOL 5-Dimension questionnaire (EQ-5D) (Rabin and Charro, 2001), the Short Form-6 Dimension (SF-6D) (Brazier et al., 2002), and the Health Utilities Index Mark 2 and Mark 3 (HUI2/3) (Horsman et al., 2003). The generic preference-based measures of HRQOL are commonly used in the economic evaluation of health interventions as they provide a multidimensional description of health that is combined with survival to generate quality-adjusted life-years (QALYs) (Longworth et al., 2014).

EQ-5D (Rabin and Charro, 2001) is a generic instrument widely used to evaluate HRQOL (Devlin and Krabbe, 2013). Two original versions of EQ-5D questionnaire are available: the previous version of EQ-5D-3L and the latest version of EQ-5D-5L. The EQ-5D consists of two parts: EQ-5D descriptive system and EQ-5D visual analog scale (EQ-5D VAS). The EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each dimension of EQ-5D-3L, there are 3 possible response categories; no problem, moderate problem, and severe problem, resulting in 243 health states. For example, the health state of 11223 indicates that there is no problem (level 1) in the dimension of mobility and self-care, having moderate problem (level 2) in the dimension of usual activities and pain/discomfort, and having severe problem (level 3) in the dimension of anxiety/depression. The EQ-5D-5L descriptive system provides 5 possible response categories. For instance, mobility asking about walking, the response is either no problems (level 1), or slight problem (level 2), or moderate problem (level 3), or severe problems (level 4), or unable to walk/extreme problems (level 5). EQ-5D descriptive system can be reported as either a health profile or a weighted index. The health profile is usually presented in a frequency table of health states obtained or in a frequency table presenting the proportion of health states in each dimension by levels. The weighted index is obtained by converting each EQ-5D health state into a single summary index format called EQ-5D index score or utility. The EQ-5D VAS records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints are labeled as 'best imaginable health state' and 'worst imaginable health state'. The scale ranges from 0 for the worst health state to 100 for the best health state. This information can be used as a quantitative measure of health outcome as judged by the individual respondents (Oemar and Oppe, 2013; Oemar and Janssen, 2013).

Many studies had been conducted to evaluate the quality of life of patients with cervical cancer in many settings using either the specific instruments (Goker et al., 2011; Azmawati et al., 2014) or generic instruments (Lang et al., 2010; Murasawa et al., 2014) and presenting the report as either a health profile in the format of score of each dimension of patient health status (Lang et al., 2010; Goker et al., 2011; Azmawati et al., 2014) or utility scores (Lang et al., 2010; Murasawa et al., 2014). Utility can be converted from EQ-5D health states using a country-specific scoring algorithm and value sets. Utility score is valuable in economic evaluation study as it is required

to calculate quality adjusted life years (QALY), which is outcome in cost utility analysis (CUA) (Drummond and Torrance, 2005). Utility generally ranges from 0 (death) to 1 (perfect health).

Presently, there has been very rare study on health-related quality of life in Indonesia. The existing study had assessed the quality of life of patients with cervical cancer in Indonesia using the generic instrument of Short Form (SF-36) and the specific instrument of EORTC QLQ-C30 and presented the report as health profile (Perwitasari et al., 2012). No study has been done to examine the utility scores among cervical cancer in Indonesia before. To the best of our knowledge, this is the first study to evaluate the HRQOL of patients with cervical cancer in Indonesia using the EQ-5D-3L.

## Materials and Methods

### Subjects

This research was a cross-sectional study. A convenient sample of 87 patients with cervical cancer who received care at Dr. Sardjito hospital, a referral hospital, in Yogyakarta, Java Island, Indonesia in the period of June to December 2013 were asked to participate in the study. We recruited all patients who were able to cooperate. Informed consents were also asked to patients before interviewing.

### Data collection and analysis

We conducted a face-to-face interview and reviewed patients' medical records to gain information regarding their socio-demographics and clinical characteristics. The following patients' characteristics were gathered: age, cancer stage, education level, employment status, marital status, and duration of illness. We classified cancer stage based on the FIGO system formulated by the International Federation of Gynecology and Obstetrics (Quinn et al., 2006). HRQOL was evaluated using the EQ-5D-3L instrument in Indonesian language version. The EQ-5D-3L official language of Indonesia is provided by the EuroQol Group (EuroQol Group, 2015). Utility (EQ-5D index score) values were calculated using the Malaysia value set (Md Yusof et al., 2012). The Malaysia value set was selected based on such considerations as geographic proximity and the similarity in demographic backgrounds, social-cultural values, and economic system to Indonesia. These considerations are recommended in selecting other country value set to be used for converting local health states to utility scores (Norman et al., 2009; Bailey and Kind, 2010). Descriptive analysis was used to present the HRQOL in terms of patients' health state, VAS and utility scores.

### Ethical consideration

The study gained the ethical approval from the Medical and Health Research Ethics Committee (MHREC) of Faculty of Medicine, Gadjah Mada University, Indonesia with the reference number: KE/FK/369/EC.

## Results

The mean age of the patients was 51.0 years old (SD=

8.9). Most patients were married (82.6%). More than half of the patients had low education level (not passed senior high school education). Only few of patients had formal occupation (17.4%). Regarding the severity of diseases, the proportion of patients in stage I, II, III, and IV were 13.8%, 50.6%, 31.0%, and 4.6%, respectively. As for the duration of illness since the first time diagnosed, the mean duration of illness was 6.7 months (SD=9.0) (Table 1).

The most commonly health states perceived by cervical cancer patients in Indonesia was the health state of 11121 (17.2%), followed by health states of 11122 (14.9%), 11111 (13.8%), and 11112 (12.6%). There was only one patient (1.2%) reporting the health state of 33333. The health states of 11111 were mostly perceived by patients in stage I and II (11.5%). The health states of 11111 indicated that there was no problem in all dimensions of EQ-5D descriptive system. The health states of 11112 indicated that there was no problem in the dimension of mobility, self-care, usual activities, and pain/discomfort; but having

**Table 1. Patient Characteristics**

Characteristic		N (%)
Age (year)	Mean±SD	51 (8.9)
Duration of illness (month)	Mean±SD	6.7 (9.0)
Cancer stage (N=87)	I	12 (13.8%)
	II	44 (50.6%)
	III	27 (31.0%)
	IV	4 (4.6%)
Education level (N=80)	Not attending school	13 (16.2%)
	Elementary school	34 (42.5%)
	Junior high school	9 (11.3%)
	Senior high school	19 (23.8%)
	University degree	5 (6.2%)
Employment status (N=86)	Unemployed	25 (29.1%)
	Part-time job	12 (14.0%)
	Self-employed	34 (39.5%)
	Paid-employed	15 (17.4%)
Marital status (N=86)	Married	71 (82.6%)
	Single	15 (17.4%)

\*N=number of patients; SD = standard deviation

**Table 2. Patients' Responses to EQ-5D Descriptive System in Each Dimension**

Dimension	No problem		Moderate problem		Severe problem	
	N	%	N	%	N	%
Mobility	67	77.0	14	16.1	6	6.9
Self-care	73	83.9	9	10.3	5	5.8
Usual activity	58	66.7	25	28.7	4	4.6
Pain/discomfort	28	32.2	48	55.2	11	12.6
Anxiety/depression	37	42.5	36	41.4	14	16.1

\*EQ-5D = Euro Quality of Life five dimension; N = number of patients

**Table 3. Descriptive of EQ-5D VAS Score and EQ-5D Index Score Classified by Cancer Stage**

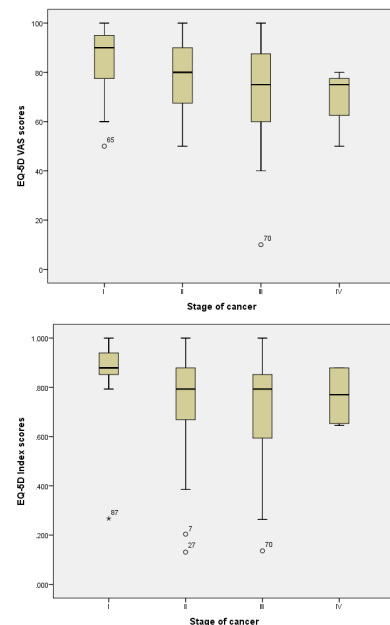
Cancer stage	EQ-5D VAS scores					EQ-5D index scores				
	Mean	SD	95% CI of mean		SE	Mean	SD	95% CI of mean		SE
			Lower	Upper				Lower	Upper	
I	84.2	15.8	74.1	94.2	4.56	0.85	0.19	0.73	0.97	0.06
II	76.4	14.8	71.9	80.9	2.23	0.76	0.2	0.7	0.83	0.03
III	72.0	20.5	63.9	80.1	3.94	0.71	0.21	0.63	0.79	0.04
IV	70.0	13.5	48.5	91.6	6.77	0.77	0.13	0.56	0.97	0.07
All stages	75.8	17.0	72.2	79.5	1.83	0.76	0.2	0.71	0.8	0.02

\*EQ-5D=Euro Quality of Life five dimension; VAS=visual analogue scale; 95%CI=95% confidence interval; SD=standard deviation; SE=standard error

moderate problem in the dimension of anxiety/depression. The health states of 11121 indicated that there was no problem in the dimension of mobility, self-care, usual activities, and anxiety/depression; but having moderate problem in the dimension of pain/discomfort. The health states of 11122 indicated that there was no problem in the dimension of mobility, self-care, and usual activities; however, having moderate problem in the dimension of pain/discomfort and anxiety/depression. Lastly, the health states of 33333 indicated that the patient having severe problem in all dimensions of EQ-5D descriptive system, including dimensions of mobility, self-care, usual activities, pain/discomfort, and of anxiety/depression. The health states reported by patients indicated that most of cervical cancer patients in Indonesia reported having no problem and moderate problems in EQ-5D descriptive system dimensions.

Descriptive statistics of EQ-5D health states showed that the most frequently reported problems were pain/discomfort (67.8%), followed by anxiety/depression (57.5%), usual-activity (33.3%), mobility (23%), and self-care (16.1%) (Table 2). The mean of VAS score was 75.8 (SD = 17.0), while the mean of utility scores was 0.76 (SD = 0.20).

The VAS scores tended to decrease by cancer stage



**Figure 1. Box Plots of the Distribution of EQ-5D VAS Scores and EQ-5D Index Scores by Cancer Stage.** The horizontal line is the median, the ends of the box are the upper and lower quartiles, and the vertical lines are the full range of values in the data

from stage I, II, III, and IV which the mean (SD) were 84.2 (15.8), 76.4 (14.8), 72.0 (20.5), and 70.0 (13.5), respectively. The utility scores also tended to decrease from stage I, II, III. However, the utility score of patients in stage IV was higher than that of stage II and III. The mean (SD) of utility scores were 0.85 (0.19), 0.76 (0.20), 0.71 (0.21), and 0.77 (0.13) for cancer stage I, II, III, and IV, respectively (Table 3). Additional of distribution of VAS and utility scores was also presented in box plots in Figure 1. The box plots showed the median; the minimum, maximum, and full range of values in the data; and the upper and lower quartiles (75th and 25th percentile).

## Discussion

The EQ-5D health states of cervical cancer patients showed that the most frequently reported problems were pain/discomfort and anxiety/depression. This study finding was similar with what was found by previous study in Indonesia (Perwitasari et al., 2012). In this study which conducted at the same setting as our study, on HRQOL of gynecologic cancer, of which 64.5% had cervical cancer, also reported the problem of health status related to pain/discomfort and anxiety/depression. The symptom score of bodily pain as measured using SF-36 was the most common health problem, while, the symptom scores of pain and insomnia as measured using EORTC QLQ-C30 indicated the moderate health problem (Perwitasari et al., 2012). These findings were also similar to what was found in other Asian settings that employed EQ-5D. In a study conducted in Singapore, the proportion of patients reporting health problem in pain/discomfort and anxiety/depression were 54.5% and 41.2%, respectively (Gao et al., 2009); while in a study conducted in Taiwan, the proportion of patients reporting health problem in pain/discomfort and anxiety/depression were 39.5% and 33.3%, respectively (Lang et al., 2010).

Furthermore, our findings were in line with those of other countries using different HRQOL instruments. For instance, in Turkey, it was reported that pain, measured using EORTC QLQ-C30 and FLIC, and insomnia, measured using EORTC QLQ-C30, were the highly-scores of symptoms (Goker et al., 2011; Akkuzu et al., 2014). In Malaysia, pain scores measured using EORTC QLQ-C30 and CX-24 were the highest score of symptom among other health status (Azmawati et al., 2014). Same pattern of high problem related to pain and anxiety also occurred among patients with other types of cancers such as breast cancer (Gao et al., 2009; Matalqah et al., 2011), colorectal cancer, head and neck cancer, lung cancer (Gao et al., 2009), and cancer in general (Tan et al., 2013). Our study is also in line with other review studies (Linden et al., 2012; Marcus, 2011). Based on the review study, the prevalence of pain and anxiety in cervical cancer was about 60% and 70%, respectively (Linden et al., 2012).

The contributors to cancer pain were investigated to be the cancer disease itself (68%), cancer treatment (18%) and non-cancer health condition (16%) (Marcus, 2011). If not managed, pain in cancer could link to emotional distress that leads to depression and anxiety (Galloway et al., 2012), which finally worsen patient's quality of life.

Anxiety in cancer patients is contributed by following factors: predisposing factors such as history of anxiety or trauma, avoidant coping style, social isolation, and life roles/caregiver; cancer-related fears; disease and treatment factors; and comorbid symptom burden such as pain, insomnia, fatigue, dyspnea, and depression (Traeger et al., 2012).

Cervical cancer had negative effect on HRQOL. Therefore, effort should be made to improve HRQOL of cervical cancer patients especially in term of pain/discomfort and anxiety/depression reduction. Some interventions for improving quality of life of cancer patients in general and specific symptoms management had been investigated and had been published elsewhere (Ezat et al., 2012; Lee et al., 2014; Nazik et al., 2014). In national level, the efforts consisted of development of national cancer control program and cancer research, existence of national cancer registry and involvement of non-government organizations. Those strategies aimed to ensure appropriate implementation of cancer management in the country (Ezat et al., 2012). Another study reported that social support; particularly from family was related to better quality of life in gynecologic cancer (Nazik et al., 2014). Moreover, the intervention of doctor-patient communication was found to have significant association with quality of life of cancer patient (Zhao et al., 2014). In term of pain symptom reduction, patient-based education management can also reduce pain in cancer patients. The education included improving the knowledge of the different methods of pain control, assessment, and methods of expression. The education purpose is to select the most appropriate pain management according to the guidelines and based on patient condition (Lee et al., 2014). Meanwhile, evidence-based recommendations to prevent and reduce anxiety in cancer patients were as follows: cognitive and behavioral interventions, relaxation training, supportive counseling, and education; as well as pharmacologic interventions using medications such as anxiolytics and antidepressants (Traeger et al., 2012).

According to the review, the utility scores of cervical cancer patients varied across country. Our study found that the mean (SD) utility score was 0.76 (0.20). The utility scores of cervical cancer patients measured using the same instrument of EQ-5D-3L in China indicated the mean (SD) utility scores of cervical cancer patient at 1, 3, and 6 months after therapy were 0.68 (0.32), 0.75 (0.31), 0.86 (0.11), respectively (Zhao et al., 2014). Meanwhile, the mean (SD) utility scores of Taiwanese cervical cancer patients were 0.84 (0.22) (Lang et al., 2010). The lower utility scores of cervical cancer samples were found in Italian patients with the mean (SD) was 0.58 (0.31) (Marcellusi et al., 2015) as well as in Argentina respondents with the mean (SD) was 0.40 (0.03) (Galante et al., 2011). The differences of utility scores could be caused by the differences of health perception across different ethnicity of population. Previous studies reported the differences of HRQOL scores among different ethnicities (Lahana and Niakas, 2013; Jhita et al., 2014). Another factor that leads to the differences of utility scores is the difference of value sets used in converting health states into utility scores in those studies. Even though the different sample groups

have the same EQ-5D health states, the utility scores might be different due to the different in value sets used (Galante et al., 2011). In addition, different utility scores could be caused by the different type of respondents. It was found that the Argentina study used general population (Galante et al., 2011) while Indonesia study used cervical cancer patients. The utility scores of Taiwanese patients was slightly higher compared to Indonesian patients since most of respondents in Taiwan study were cervical cancer patients in stage I and II (94.2%) (Lang et al., 2010).

Our study also found that the EQ-5D VAS and utility scores tended to decrease from cancer stage I to stage IV. However, the utility score in cancer stage IV was higher than that of stage II and III. This could be due to the small sample of patients in stage IV (n=4). The mean (SD) EQ-5D utility scores of cancer stage I, II, III, and IV in this study were 0.85 (0.19), 0.76 (0.20), 0.71 (0.21), and 0.77 (0.13), respectively. The mean (SD) EQ-5D utility scores by cancer stage in Japanese sample were 0.80 (0.15), 0.78 (0.11), 0.64 (0.15), 0.63 (0.15), 0.71 (0.15), 0.50 (0.17), 0.52 (0.17), 0.21 (0.28) for cancer stage IA1, IA2, IB1, IB2, IIA, IIB, III, and IV, respectively (Murasawa et al., 2014). The utility scores of Indonesian sample were higher as compared to Japanese sample. Again, the difference could be caused by the different types of participants and different value sets used to calculate the utility. Our study was conducted in cervical cancer patients, while Japanese study was conducted in healthy female (without cervical cancer disease) who were asked to perceive hypothesized health states (Murasawa et al., 2014). The general population was more likely to over-emphasize the health perceived status of such disease scenario (Wilson et al., 2000; Percy et al., 2008). Hence, the utility scores of hypothesized sample (Japanese respondents) tended to be lower than that of the real cervical cancer patient (Indonesian respondents).

It is important to note the limitation of our study. Our sample size was relatively small and based on a convenience sampling method of cervical cancer patients with access to health care facilities in an urban area of Yogyakarta. Therefore, generalization should be made with caution. Further study should be conducted using a larger sample size using random sampling method. Utility was calculated using other country value set that might not represent actual perception of Indonesian population.

In conclusion, this study confirmed that cervical cancer had negative impact on HRQOL. Most health problems reported were pain/discomfort and anxiety/depression. In addition, this study provided the utility scores of Indonesian sample with cervical cancer that could be used for future economic evaluation studies.

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