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Health-Related Quality of Life of Patients with HPV-Related Cancers in Indonesia

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ABSTRACT

Background: Human papillomavirus (HPV)-related cancers are a serious concern in developing countries. Valid estimates of a country-specific health-related quality of life (HRQOL) for patients with HPV-related cancers provide a substantial tool in determining the burden of the disease. **Objectives:** To investigate the HRQOL of patients with HPV-related cancers in Indonesia. **Methods:** The HRQOL of patients with HPV-related cancers (cervical, uterine, nasopharyngeal, head and neck, and anogenital cancer) was assessed using the EuroQol five-dimensional questionnaire (EQ-5D). Validity and reliability were assessed by means of construct validity and test-retest reliability methods, respectively. Subsequently, the EQ-5D utility index was calculated using the Thailand value set. **Results:** The EQ-5D came out as a valid and reliable questionnaire for measuring the HRQOL of patients with HPV-related cancers in Indonesia. From a total of 520 patients diagnosed with HPV-related cancers, 404 patients were excluded because of not fulfilling the inclusion criteria, and so 116

patients finally participated in the study. The mean age of the patients was 47.5 ± 12.03 years. Most of the patients were women (56.0%) and married (97.4%), and less than half of them had finished high school (32.7%). Moreover, the proportions of nasopharyngeal, cervical, head and neck, anogenital, and uterine cancers in the study population were 29.3%, 24.6%, 22.4%, 14.2%, and 9.5%, respectively. The average HRQOL of the patients with HPV-related cancers was 0.69 ± 0.10 , with the highest and lowest estimates applying to uterine cancer (0.84 ± 0.29) and head and neck cancer (0.58 ± 0.33), respectively. **Conclusions:** The HRQOL of patients with HPV-related cancers was found to be reduced to a certain extent in our study for Indonesia.

Keywords: cervical cancer, health-related quality of life, HPV-related cancer, human papillomavirus, Indonesia.

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Introduction

Human papillomavirus (HPV) infections are a well-established cause of not only cervical cancer [1–4] but also other cancers, including head and neck, anogenital (anus, vulva, vagina, and penis), uterine, and nasopharyngeal cancers [5,6]. In addition, the global burden of HPV-related cancers is increasing, and developing countries, including Indonesia, bear a high proportion of this burden [7]. For example, data reported by the Ministry of Health in Indonesia showed that HPV-related cancers, especially cervical and nasopharyngeal cancers, were among the 10 cancers with the highest incidence and mortality rate in Indonesia [8].

Various health technologies such as chemotherapy [9,10], prevention strategies [11–14], new hormonal therapies [15,16], and clinical practice guidelines [17] are constantly developed and changed to combat cancer. The implementation of these health technologies has resulted in a wide range of improvements in outcome measures, with success being influenced by cancer type, study site, outcome measure, or even the cancer treatment and prevention itself [18,19]. Nevertheless, various, and sometimes life-threatening, side effects from the treatments could possibly occur, and the health technologies as well as their side effects occasionally influence not only the health status of the patients but also their social and emotional well-being.

Conflicts of interest: D. Setiawan has received the Directorate General of Higher Education Scholarship, Ministry of National Education, Indonesia. M. J. Postma reports grants and personal fees from various pharmaceutical industries, potentially not interested in the subject matter, during the conduct of the study; grants and personal fees from various pharmaceutical industries, potentially not interested, outside the submitted work; and 3% of stocks of Ingress Health. A. Dusafitri, G. F. Galistiani, A. D. I. van Asselt declare that they have no conflicts of interest. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Within this broad variety of issues, the need for comparability of outcomes has been recognized and the term “health-related quality of life” (HRQOL) for this purpose is widely accepted [20,21]. HRQOL generally captures the complete health state of an individual because it includes several important health parameters from, for example, the physical, psychological, and social health dimensions [22]. Any reduction in the value of HRQOL reflects a reduction in the health of the individual. Therefore, HRQOL is able to convey important information for assessing the overall burden of a disease and the effectiveness of interventions as well.

With regard to cancer disease, HRQOL measurement tools may be classified as *generic*, *general cancer*, *cancer-site-specific*, and *cancer-problem-specific*. General cancer, cancer-site-specific, and cancer-problem-specific HRQOL measurement tools generally provide more detailed information in a single cancer-type or cancer-related problem, whereas an ultimate advantage of generic HRQOL measurement tools is that because they can be implemented over a wide range of conditions and interventions, they enable comparison of outcomes across diseases [23,24]. One example of a generic questionnaire is the EuroQol five-dimensional questionnaire (EQ-5D), which was developed by the EuroQol group and is widely used across the world [25–27]. Further advantages of the EQ-5D are that it has only five questions and it is easy to administer and complete. The EQ-5D is of two types: the three-level EQ-5D (EQ-5D-3L) and the more recently developed version with five levels (EQ-5D-5L). Several studies support both the validity and the sensitivity of the EQ-5D in patients with cancer [24,28]. Nevertheless, some studies suggest that the EQ-5D-5L has less ceiling effects and better discriminative abilities with potentially more power to detect differences between groups as compared with the EQ-5D-3L [29,30].

Indonesia-specific HRQOL of HPV-related cancers provides initial information in decision-making processes because it will assist subsequent processes such as cost-utility analyses. Subsequently, this will allow for comparing outcomes of interventions for HPV-related cancers with the outcomes of other interventions, within as well as outside the area of HPV-related cancers. The purpose of this study was to investigate the HRQOL of patients with HPV-related cancers in Indonesia using the EQ-5D-5L.

Methods

A descriptive cross-sectional study was conducted, directed at the HRQOL of patients with HPV-related cancers in Indonesia. The study was divided into two main activities, consisting of pilot testing and the main study. Notably, this study was approved by the ethics committee of the Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia.

Pilot Study

Initially, a pilot study was conducted to evaluate the validity and reliability of the EQ-5D for patients with HPV-related cancers in the specific Indonesian setting. A convenience sample of 30 patients with HPV-related cancers was recruited from Dadi Keluarga Public Hospital, Purwokerto, Indonesia. On the recruitment day (day 0), patients filled out both the EQ-5D-5L and the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire C30 (EORTC QLQ-C30), a cancer-specific questionnaire. On day 14, patients filled out the EQ-5D-5L a second time.

As mentioned, the EQ-5D is a generic quality-of-life instrument developed by the EuroQol group and contains five questions and a visual analogue scale (VAS). The questions comprise five

different dimensions, that is, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. We adopted the updated version of the EQ-5D containing five levels of severity on each dimension because it was considered to be more sensitive and reliable compared with the previous three-level version (EQ-5D-3L). In addition, the VAS records a patient's self-rated health perception, graded between 0 (worst) and 100 (best).

The EORTC QLQ-C30 is a disease-specific questionnaire developed mainly to assess the quality of life of patients with cancer. It consists of three different scales: functional (15 questions), symptoms (13 questions), and global quality of life (2 questions). The EORTC QLQ-C30 was chosen as the comparator in the validation process because the Indonesian version has been validated [31] and some questions, particularly on global health status, physical function, role function, emotional function, and pain, have been identified as significant predictors of the EQ-5D outcomes according to several mapping studies [32–35]. Therefore, construct validity testing, that is, assessing whether the EQ-5D can be interpreted as a meaningful measure of quality of life, was performed by measuring the correlation between each mapped question of the EQ-5D and the EORTC QLQ-C30 because they have the same construct (convergent validity method) [36]. Each of the EORTC QLQ-C30 subscales was considered to be correlated with an EQ-5D dimension when the statistically significant Pearson correlation coefficient indicated so [32,34,35]. Furthermore, the value of the Pearson correlation coefficient represents the magnitude and the direction of the correlation [37].

To ensure the reliability of the EQ-5D, the two measurements (day 0 and day 14) were compared within patients to assess test-retest reliability [38]. This method was chosen because in patients with cancer, significant changes in quality of life rarely occur within a 14-day interval and although a clear recommendation to avoid recall bias is scarcely available and often debatable, this 14-day interval is considered sufficient to avoid recall bias [39]. Test-retest reliability represents measurement stability, using intraclass coefficients (ICCs) [40,41]. ICC values were interpreted as follows: weak agreement if the ICC is lower than 0.40, good agreement if the ICC lies between 0.40 and 0.75, and excellent agreement if the ICC is 0.75 or higher [41]. In addition, the Cronbach α was calculated to assess internal consistency, that is, to determine whether the EQ-5D questions together measure the same construct of the HRQOL of patients with HPV-related cancers. Internal consistency was considered to be good if the Cronbach α was higher than or equal to 0.80 [38].

Main Study

All registered patients from 2010 to 2015 in Margono Public Hospital, Purwokerto, Indonesia, were screened for their eligibility. Inclusion criteria were as follows: patients were older than 18 years, were diagnosed with any HPV-related cancer (cervical, uterine, nasopharyngeal, head and neck, or anogenital cancer), and had received any care in the hospital. Patients with chronic disease comorbidity were excluded. A clinical convenient sample was implemented for all patients who were eligible and received and signed informed consent before both the EQ-5D and the EORTC QLQ-C30 were filled out while the patient's sociodemographic and clinical information, such as age, sex, education level, and diagnosis of cancer, were collected from medical records. These two separate data sets were matched according to the medical record number for each patient.

Each dimension of the EQ-5D-5L is presented as a dichotomous outcome: no problem (answer level 1) or problems (answer levels 2–5). Furthermore, a major outcome provided by the EQ-5D

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