

## Health Related Quality of Life and Residual Symptoms in Prostatic Surgical Treatment at Bethesda Hospital Yogyakarta: a Retrospective Study

Daniel Mahendra Krisna,<sup>1</sup> Hariatmoko,<sup>2</sup> Rizaldi Taslim Pinzon<sup>1</sup>

<sup>1</sup>Faculty of Medicine Duta Wacana Christian University Yogyakarta, <sup>2</sup>Department of Surgery Bethesda Hospital Yogyakarta

### Abstract

**Background:** The incidence of Prostate Enlargement (PE) has been increasing over the years. The satisfaction towards the treatment result and life quality (QOL) improvement must be the key point of PE treatment. QOL is affected by many conditions, such as age, socioeconomic status, comorbid disease, and type of surgery. The objective of the study was to assess the QOL in PE patients post surgery, to explore the predictor factor, and to assess the satisfaction related to urinary functionality in the Indonesian context.

**Methods:** A retrospective study was conducted and the subjects were all PE patients who underwent surgical treatment. EQ-5D-5L/EQ-VAS and Index Quality of Life (IQL) were used to assess the patient's QOL & treatment satisfaction. The subjects were divided into several sub-groups based on age, type of surgery, comorbid condition, type of ward, funding source, histopathological result, and the year of treatment. The collected data were analyzed using Mann-Whitney test, Kruskal Wallis test, or Chi-square test, Spearman's rho test and multiple linear regression.

**Results:** All the 149 subjects were at the average age of 69.09 years. There were no significant statistical differences in QOL between age, comorbid conditions, and histopathology result. Health insurance (HI) was significantly associated with QOL. There were improvements of IQL subjects. The most symptoms remaining was frequency (47.4%).

**Conclusions:** Life improvement must be the major purpose of PE therapy. The association between HI with QOL suggests that a better HI in developing countries can ensure a better quality of life outcome.

**Keywords:** Health-related Quality of Life, prostate enlargement, surgery

### Introduction

Prostatic enlargement either Benign Prostate Hyperplasia (BPH) or Prostate Cancer, is the most common urologic disorder in the elderly population.<sup>1</sup> The incidence of BPH has been increasing over the years. The risk of BPH increases with age and several studies have shown that BPH incidence is as high as 90% in people over 70 years old.<sup>2</sup> Prostate cancer prevalence in Indonesia was 0.2% in 2013 which equals to 25,012 patients. This makes prostate cancer the second most common high-mortality rate disease experienced in Indonesia.<sup>3,4</sup>

The BPH usually is not a life threatening disease, but rather affects people's quality of life (QOL). Therefore the primary goal of

treatment should be improving the patient's QOL,<sup>1</sup> especially related to social activities and general feeling of well-being. The QOL affected by many conditions, such as age, socioeconomic status, comorbid disease, and type of surgery.<sup>5,6</sup> Health Related Quality of Life (HRQOL) assessment tools can be used to evaluate patient satisfaction before and after treatment. There are several questionnaires used to evaluate patients HRQOL in patients who suffer from prostate disease such as the International Prostate Symptom Score (IPSS); Sexual Functioning Index (SFI); BPH Impact Index (BII) and EQ-5D Index (EQ-5D Index).<sup>7-9</sup>

The diagnosis and treatment of prostatic enlargement disease have made significant advances in past years. The gold standard of radical prostatectomy has nowadays been

**Correspondence:** dr. Daniel Mahendra Krisna, Faculty of Medicine, Duta Wacana Christian University Yogyakarta, Jalan Dr. Wahidin Sudirohusodo no 5-25 Yogyakarta, Indonesia, Email: danielkrisna24@yahoo.com

largely replaced by endourological treatment. For example, Transurethral Resection of the Prostate (TURP), when compared to radical prostatectomy and medical treatment is far less invasive, and is associated with fewer complications, shorter hospitalization, better outcomes, better quality of life improvement and reduced cost.<sup>10</sup>

Both medical and surgery treatments are known to increase the HRQOL of patients with prostatic disease, especially those who have moderate-severe lower urinary tract symptoms (LUTS) but no significant difference in effect is observed between the two modalities.<sup>8,11,12</sup> In addition HRQOL is affected by other factors such as culture and geographic area. It has been shown that HRQOL differs between European and Asian men with Hepatocellular Carcinoma<sup>13</sup> but no such study of HRQOL in patients with prostate disease exists.

The aim of this study was to assess the HRQOL in patients with prostatic enlargement disease post surgery, to explore possible predictor of worse HRQOL following prostatic surgery, and to assess patient satisfaction related urinary functionality post surgery, in the Indonesian context.

## Methods

This study evaluated BPH surgical data recorded by medical records at Bethesda hospital, Yogyakarta. The subjects were all patients with BPH and/or prostate cancer who underwent surgical treatment, either TURP or Radical Prostatectomy, in the period of January 2014–January 2016. The study was approved by the Ethics Committee of the Faculty of Medicine, Duta Wacana Christian University. Data collection included age, phone number, address, admission date, date of surgery, date of hospital discharge, type of surgery, comorbid conditions, ward type, funding source, histopathological result, and functional status. The outcomes were followed up by phone interviews.

Subjects were asked to answer the questionnaire over the phone. Exclusion criteria were those patients with incomplete medical data, those who did not answer the phone or had passed away.

The EQ-5D-5L/EQ-VAS was used to assess the subject's HRQOL. EQ-5D-5L is an international questionnaire consisting of 5 questions that evaluates mobility, self-care, daily activity, pain, and depression. Each item is evaluated using a 5 point Likert scale

with answers ranging from 1 to 5 points (no problems, slight problems, moderate problems, severe problems, and extreme problems).

The summary index was calculated using the EQ-5D-5L Crosswalk Index Value Calculator. This tool was downloaded from the EuroQol website. The EQ-5D-5L index ranges from 1 (full health related quality of life) to 0 (death).<sup>15</sup> The specific values were derived from Thailand samples because there were no specific sets available for the Indonesian population.

EQ-VAS (Visual Analog Score) was used to evaluate the health related quality of life using the subject's personal assessment, ranging from 0 (worst health state) to 100 (best health state). Permission for the use of this instrument in the study was granted by the EuroQol Group.

Furthermore, urinary function related quality of life was assessed using the Index Quality of Life questions in IPSS (IPSS-Q8). The question "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?" was translated into Indonesian language accounting for the fact that a few people speak English. The subjects were asked to recall their feelings 3 months post surgery, 6 months post surgery, and on the day of the phone call. The question was answered according to a 7 point Likert scale, with 1 being 'Delighted' 2: 'Pleased', 3: 'Mostly Satisfied', 4: 'Mixed', 5: 'Mostly Dissatisfied', 6: 'Unhappy', and 7: 'Terrible'.

The possible factor of worse EQ-5D-5L was assessed by dividing them based on the following sub-group: 1) Age ( $\leq 60$  y.o. vs  $> 60$  y.o.), defined as age when surgery was performed. The group was divided based on WHO and Indonesian law definition of elderly, 2) Comorbid (With Comorbid vs Without Comorbid), defined as the presence of one or more additional disease, 3) Type of Surgery (Open Prostatectomy vs TURP), defined as the surgery technique which was used as PE treatment, 4) Functional status, was based on Instrumental activities of daily living (IADL), 5) Funding Source (Family vs ASKES/BPJS (National Health Insurance), vs BUMN (State-Owned Enterprise), vs other), represented the socioeconomic status, 6) Ward Type (class 1 vs class 2 vs class 3 vs VIP vs VVIP), represented the socioeconomic status and in-hospital environment, 7) Histopathological result (BPH vs Adenocarcinoma), Histopathological result was proven by specimen biopsy, and 7) Year

of Treatment (2014 vs 2015), defined as one year or two years after surgery. Besides, the frequency of answers from IQL index were also compared between 3 and 6 months post surgery and on the day when answering the questionnaire.

The sample size was determined by the  $N = [(Z\alpha + Z\beta) / C]^2 + 3$ .  $Z\alpha$  was The standard normal deviate for  $\alpha$ ,  $Z\beta$  was The standard normal deviate for  $\beta$ , and C was  $0.5 * \ln[(1+r) / (1-r)]$ . The number of samples for this study was 123 subjects. As for the statistical analysis, categorical data were presented as frequency and percentage. Continuous data were presented as a mean or standard deviation. Kolmogorov-Smirnov test was used

to determine the data distribution. Mann-Whitney test, Kruskal Wallis test, or Chi-square test was used, whether it was appropriate to assess the difference or not. The correlation between outcomes and variables were assessed using Spearman's rho test. Multiple linear regression was used to assess predictor influences. Moreover, p value less than 0.05 and p value less than 0.001 (Spearman) were considered significant.

### Results

There were 149 subjects with an average age of 69,09 years. Specifically, the youngest

**Table 1 Subject's Characteristics**

Variable	Frequency (n)	Mean±SD	Range (years)
Age	149	69.09	52-91
	Category	Frequency (n)	Percentage(%)
Length of Stay	1-3 Days	135	90.6
	4-6 Days	10	6.7
	>7 Days	3	2
Preoperation Waiting Time	1-3 Days	12	8.1
	4-6 Days	96	64.4
	>7 Days	40	26.8
Type of Ward	Class 1	36	24.2
	Class 2	22	14.8
	Class 3	44	29.5
	Class VIP	36	24.2
	Class VVIP	1	0.7
Funding Source	Family	50	33.6
	NHI	71	47.7
	DHI	7	4.7
Functional Status	Others	11	7.4
	Fully active	141	94.6
	Restricted activity	4	2.7
Type of Surgery	Partial dependent	3	2
	Completely disabled	1	0.7
	Radical Prostatectomy	11	7.4
Histopathology Result	TURP	138	92.6
	BPH	105	70.5
	Adenocarcinoma	19	12.8

Note: VIP=Very Important Person; VVIP=Very Very Important Person; NHI=National Health Insurance; DHI=District Health Insurance; JVP=Jugular Venous Pressure; ECG=Electrocardiograph; RPM=Rate per Minute; TURP=Trans Urethral Resection of Prostate; BPH=Benign Prostate Hyperplasia

**Table 2 EQ-5D Index correlation between Variables**

Variables	Mean (SD)	p-value*	p-value**
Age			
≤ 60 years	81.2(0.174)	0.413	0.000
> 60 years	73.87(0.145)		
Comorbid Conditions			
Without Comorbid	77.7(0.178)	0.368	0.000
With Comorbid	71.87(0.165)		
Type of Surgery			
Radical Prostatectomy	74.91(0.187)	0.994	0.000
TURP	75.01(0.165)		
Functional Status			
Fully active	75.6		
Restricted activity	36.63	0.184	0.000
Partial dependent	86.83		
Completely disabled	109		
Funding Source			
Family	67.37(0.175)		
National Health Insurance	76.00(0.158)	< 0.05	0.000
District Health Insurance	37.47(0.240)		
Others	63.95(0.142)		
Type of Ward			
Class 1	68.14(0.173)		
Class 2	59.66(0.193)	0.403	0.000
Class 3	76.64(0.163)		
VIP	69.19(0.170)		
VVIP	101.5		
Histopathology result			
BPH	63.18(0.169)	0.292	0.000
Adenocarcinoma	55.24(0.181)		
Year of Treatment			
2014 (≤ 1 year)	75.71(0.167)	0.819	0.000
2015 (> 1 Year)	74.23(0.175)		

Note: p-value\*=P-value of Spearman correlation test, p-value\*\*=P-value of Kolmogorov-Smirnov test

age was 52 years, while the oldest was 91 years old. Moreover, 24.2% of subjects were patients of class 1 ward and VIP. While, 47.7% of subjects used the National Health Insurance as their funding source. Furthermore, 92.4% of subjects underwent TURP surgery with 70.5% of them showing BPH on their Histopathological result (Table 1).

About 54.4% of the subjects answered 11111 in the EQ-5D-5L questionnaire and 14.1% of them answered 11222. The results of EQ-5D showed there were moderate problems in the usual activities and anxiety components.

The EQ-5D-5L Index relationship was analyzed with each variable based on the sub-group, following age, comorbid, type of

**Table 3 Responses to EQ-5D by Variables**

Variables	n	Mobility	Self Care	Usual activities	Pain/discomfort	Anxiety/depression
<b>Age</b>						
≤ 60 years	23	70.5	72.74	70.37	65.93	72.35
> 60 years	126	75.82	75.41	75.85	76.65	75.48
p- value		0.188	0.546	0.446	0.193	0.706
<b>Comorbid Conditions</b>						
Without Comorbid	87	73.93	74.64	75.56	74.76	74.9
With Comorbid	62	76.51	75.51	74.21	75.34	75.14
p-value		0.383	0.789	0.797	0.923	0.969
<b>Type of Surgery</b>						
Radical Prostatectomy	11	77.27	76.27	70.95	80.36	72.23
TURP	138	74.82	74.9	75.32	74.57	75.22
p-value		0.66	0.822	0.66	0.611	0.795
<b>Functional Status</b>						
Fully active	141	75.26	75.31	74.94	74.94	74.59
Restricted activity	4	70.5	69.5	94.5	94.5	100.63
Partial dependent	3	70.5	69.5	57.5	57.5	70
Completely disabled	1	70.5	69.5	57.5	57.5	45.5
p-value		0.91	0.88	0.435	0.067	0.446
<b>Funding Source</b>						
Family	50	69.67	71.45	71.44	73.08	70.48
National Health Insurance	71	68.44	67.44	66.13	65.01	65.23
District Health Insurance	7	95.29	94.29	105.14	92.14	90.79
Others	11	65.5	64.5	66.05	74.09	85.41
p-value		0.001	0.003	0.01	0.169	0.105
<b>Type of Ward</b>						
Class 1	36	69.36	68.36	72.67	73.89	70.39
Class 2	22	74.98	73.98	76.2	77.75	78.48
Class 3	44	68.66	69.24	64.48	63.53	66.35
VIP	36	69.36	70.29	70.75	70.03	69.64
VVIP	1	65.5	64.5	53.5	43	43
p-value		0.683	0.841	0.541	0.429	0.646
<b>Histopathology Result</b>						
BPH	105	62.04	62.22	62.56	60.67	62.07
Adenocarcinoma	19	65.03	64.03	62.18	72.63	64.89
p-value		0.434	0.67	0.954	0.109	0.708
<b>Year of Treatment</b>						
2014 (≤ 1 year)	78	74.32	74.28	75.53	73.24	75.47
2015 (> 1 Year)	71	75.75	75.8	74.42	76.93	74.49
p-value		0.625	0.635	0.832	0.536	0.87

**Table 4 Multiple Analysis Regression between EQ-5D Index with Variables**

Variables	p-value
Age	0.094
Comorbid Conditions	0.352
Type of Surgery	0.46
Functional Status	0.256
Funding Source	0.162
Type of Ward	0.357
Histopathology Result	0.215
Year of Treatment	0.298

surgery, functional status, funding source, ward type, histopathological result, and year of treatment (Table 2 and 3). Kolmogorov-Smirnov normality test was used to determine data distribution in all variables ( $p=0.000$ ). Based on EQ-VAS measurement, this study discovered that the average of VAS results in male population aged 40-49 years was 78,3, aged 50-59 years was 75,5, while aged 60-69 years was 72. The mean of EQ-5D VAS was 74.06 and standard deviation was 6.350.

Furthermore, the EQ-5D index correlation between variables showed age below 60 years, subjects without comorbid, used national health insurance as the funding source, and histopathological result with changing BPH had higher average compared to their comparators, but was not statistically significant (Age 81.2 vs 73.87,  $p=0.413$ ; Comorbid condition 77.8 vs 71.87,  $p=0.368$ ; Type of surgery 74.91 vs 75.01,  $p=0.994$ ; Functional status 75.6 vs 36.63 vs 86.83 vs 109,  $p=0.184$ ; Type of ward 68.14 vs 59.66 vs 76.64, vs 69.19 vs 101.5,  $p=0.184$ ; Histopathology result 63.18 vs 55.24,  $p=0.292$ ; Year of treatment 75.71 vs 74.23,  $p = 0.819$ ).

The funding source was the only variable that was statistically significant different (Funding source 67.37 vs 76.00 vs 37.47 vs 63.95,  $p<0.05$ ). The result was similar when we assessed variables to each EQ-5D components. There was no relationship between each variables (Table 4).

Moreover, the subjects' IQL-IPSS-Q8 correlation based on the period were: 3 months after surgery, 6 months after surgery, and the recent condition during filling out the questionnaire revealed that there was an increase of "pleased" and a decrease of "mostly dissatisfied" answers from 3 months after surgery to the recent condition during filling out the questionnaire. In addition, an increase of urinary frequency (47.4%), nocturia (21.1%), and dysuria (10.5%) became the most frequent complaints post surgery (Table 5).

## Discussions

The average age of subjects in this study was 69.06 years. This was in line with the rate of

**Table 5 Bothersome Symptoms in the Follow-up after Surgery**

Variable	Frequency (n)	Percentage (%)
Frequency	18	47.4
Nocturia	8	21.1
Dysuria	4	10.5
Hematuria	2	5.3
Obstruction	2	5.3
Erectile Dysfunction	1	2.6
Urgency	2	5.3
Retrograde Ejaculation	1	2.6

life expectancy in 2012 (70,1 years).<sup>3</sup> The definition of elderly varied in each country. According to WHO, elderly means male or female aged over 60 years. The subjects were divided into several categories, including age. The number of subjects aged over 60 years was the majority. This was surely in accordance with the incidence of prostate enlargement that increase in the age of over 60 years.<sup>16,17</sup> Almost all of the subjects (32%) only experienced less than 3 days hospitalization and brought the catheter along to their home. This was shorter than in the study of Khan<sup>18</sup>, which has found that the average duration of hospitalization is 3.5 days. Changes in the urine color to clearer one, or urine is free from visible blood trace, may be the indicator of the patients' hospital discharge.<sup>19</sup> It might occur to almost all of the subjects who used the National Health Insurance (ASKES/BPJS) as their funding source, which highly affected their duration of hospitalization since it could decrease the patients' total charge.

There were different EQ-5D-5L average between age (sub-group) and comorbid, even though it was not statistically significant. Mobility impairment, previous history of stroke, respiratory disorder, and cardiovascular disease such as hypertension played a critical role in affecting the patients' quality of life after surgery, both surgical and medical. This finding is obviously in accordance with the study conducted by Cortez-Diaz et al.<sup>19</sup> Furthermore, the funding source became the only variable that significantly affected the patients' quality of life. This fact shows that patients living in developing countries such as Indonesia, where most of the citizen depends on the national health insurance, really need such assurance to get the best medication from government programs so that they can reach their therapy targets. Again, this fact is supported by a study conducted by Jo et al.<sup>20</sup> which revealed that the influence of status of social-economy, culture, ethnic, and religious background is real. The subjects' VAS correlation based on sub-group with populations, generally could help the researcher to interpret the result.

This study discovered that the EQ-VAS was lower than the general population which is in line with what Cortez-Diaz et al.<sup>11</sup> has found. This fact showed that prostate enlargement affects the patients' quality of life.

Furthermore, there was a clear change in the IQL questionnaire. The "pleased" answer of 3 months post surgery with recent condition on the day when answering the questionnaire showed a degree of increase, while the

"mostly dissatisfied" answer experienced the opposite. However, as the subjects had not reached their better condition yet at the time the researcher gave the questionnaire, there was a change over the 6 months after surgery, such as the decrease in "pleased" answer and increase in "mostly satisfied" answer. This was due to the clinical perception of adapting or accepting urination quality by patients, or by the improvement on patients' remaining complaints after surgery. The most frequent complaint was what the patients described as overactive bladder. Even more, a subject suffered from erectile dysfunction or retrograde ejaculation.

As a conclusion, life improvement must be the major purpose of prostate enlargement therapy, especially BPH. The researcher figures out that the existing therapy can improve the patients' quality of life, even though it still has many weaknesses so the optimal therapy cannot be obtained. It is also necessary to prevent complaints that affect the patients' quality of life after surgery as much as possible. Furthermore, the government in developing countries should consider about the financial guarantee of medication, in order to establish healthy citizens with good quality of life, especially of the elderly.

The limitation of this study was the questionnaire data had been collected only via phone call so that perception or understanding over the questions could be varied in each subject. In addition, long term medication, and the number of subjects living outside the city were considered as the obstacle which occurs in this study. However, this study has several advantages to point out such as: it was conducted in Indonesia as one of the developing countries in the world, and provided subjects who had undergone surgery in the previous one or two years, so that health providers could observe their patients' treatment results accordance with their quality of life.

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