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PROCENA EFEKATA OPERATIVNOG LEČENJA BENIGNOG UVEĆANJA PROSTATE NA SIMPTOME DONJEG URINARNOG TRAKTA I KVALITET ŽIVOTA


UDC:

DOI: https://doi.org/10.2298/VSP170227062B

When the final article is assigned to volumes/issues of the Journal, the Article in Press version will be removed and the final version appear in the associated published volumes/issues of the Journal. The date the article was made available online first will be carried over.
IMPACT OF SURGICAL TREATMENT OF BENIGN PROSTATE HYPERPLASIA ON LOWER URINARY TRACT SYMPTOMS (LUTS) AND QUALITY OF LIFE

Procena efekata operativnog lečenja benignog uvećanja prostate na simptome donjeg urinarnog trakta i kvalitet života

Short title: Impact of surgery of BPH on Qol


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Abstract

Background/Aim: Benign prostatic hyperplasia (BPH) is a pathological process, which is one of the most common causes of so-called lower urinary tract symptoms (Lower Urinary Tract Symptoms-LUTS). LUTS affect many aspects of daily activities, and almost all domains of health related quality of life (HRQoL). The objective of this study is to evaluate the effects of operative treatment of BPH using standard clinical diagnostic procedures, and effects on LUTS using the symptom-score validated to Serbian language, as well as implications on HRQoL.

Methods: 74 patients underwent surgical treatment for BPH. The study protocol included objective and subjective parameters of the following sets of variables measured before and after the surgery: voiding and incontinence symptoms were measured using ICS male SF
questionnaire, HRQoL was measured using SF-36 questionnaire, along with standard clinical measurement of residual urine and urine flow.

**Results:** After the surgery, all patients had decrease of voiding (13.5±3.3 before and 1.5±1.4 after surgery) and incontinence symptoms (5.7±3.9 before and 0.6±0.8 after surgery) scores in comparison to period before operative treatment (p< and p< respectively). Significant improvement of all dimensions of HRQoL were improved in particular emotional health. Although mental and physical total scores are significantly better then prior the surgery, the level of improvement of voiding and incontinence scores is significantly correlated only to the level of improvement of mental score.

**Conclusion:** After BPH surgery, patients will likely have normal voiding symptoms, barely some involuntary control over urination and better all dimensions of HRQoL, in particular role emotional.

**Key words:** BPH, ICS male SF, SF 36, voiding and incontinence

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**Sažetak:**

**Uvod/Cilj:** Benigno uvećanje prostate ili benigna hiperplazija prostate (BPH) je patološki proces koji vrlo često uzrokujebrojne simptome donjeg urinarnog trakta (Lower Urinary Tract Symptoms-LUTS) i posredno ometa obavljanje dnevnih aktivnosti, umanjuje kvalitet života eng. *health related quality of life* (HRQoL) muškaraca. Cilj ovog istraživanja je procena efekata operativnog lečenja BPH na LUTS i na HRQoL koja će se uraditi uz pomoć standardnih kliničkih dijagnostičkih procedura kao i primenom simptom-skora validiranog na srpski jezik. **Metode:** 74 pacijenta je podvrgnuto operativnom lečenju zbog BPH. Simptomi mokrenja i inkontinencije su mereni ICS male SF upitnikom, a kvalitet života upitnikom SF-36, i to pre i 6 meseci nakon operacije. Procena kliničkih efekata operativnog lečenja je utvrđena merenjem, toka i jačine mlaza urina tokom uriniranja i količine rezidualnog urinapre i posle operacije.

**Rezultati:** U odnosu na period pre operacije, posle operacije svi pacijenti su imali devetostruko smanjenje učestalosti mokrenja, i simptoma inkontinencije. Njihov kvalitet života je značajno poboljšan, izrazito u domenu emocionalnog zdravlja. Iako su značajno poboljšani ukupno skorovi mentalne i fizičke komponente kvaliteta života zdravlja, nivo
Introduction:

Benign enlargement of prostate, or benign prostatic hyperplasia (BPH) is a pathological process, which is one of the most common causes of the so-called lower urinary tract symptoms (Lower Urinary Tract Symptoms-LUTS)\(^1\). A multinational population-based survey point to the high prevalence of LUTS in older population\(^1\), suggesting that focus should be on finding treatment strategies of LUTS and BPH that are as efficacious, safe and manageable solution that also improves quality of life of patients\(^2\) given an increasing likelihood that man will seek help for LUTS at tributable by BPH along with a prolonged life expectancy\(^3\). LUTS affect many aspects of daily activities, and almost all health dimensions (Physical function (PF), Role Physical (RP), Body pain (BP), Global Health (GH), Vitality (Vit), Social function (SF), Role Emotional (RE), Mental health (MH))\(^4\). Among many factors attributable to LUTS\(^2\), benign enlargement of the prostate is a major clinical and public health problem\(^5\). Recent attempts to improve diagnosing of LUTS attributable by BPH include a number of questionnaires for patients in addition to standard clinical examination and diagnostic procedures to document how LUTS affects quality of patients’ life, in particular. These surveys have become an indispensable part of the algorithm tests prior decision-making about the treatment and are common element of every assessment of treatment effects\(^5\). Although the International Prostate Symptom Score (IPSS) is the most famous\(^8\), its variations are used in practice\(^9,10\) their biggest drawback is that they do- not examine the symptoms of incontinence, as it was thought that incontinence is primarily a female issue. In recent years evidences show that that men also suffer from urination difficulties and incontinence leading to the deterioration of HRQoL\(^11\). A short form of a questionnaire of the International Association for Incontinence.thoroughly and accurately defines the urinary symptoms and
incontinence\textsuperscript{9,10,12}. Additionally important is to appropriately measure the patient's quality of life and in an efficient way to provide a valid and psychometrically proper patient’s opinion and experience\textsuperscript{13}.

To evaluate the effects of operative treatment of BPH on LUTS and on HRQoL in this study apart from standard clinical diagnostic procedures, the new symptom-score standardized instruments were applied: SF-36\textsuperscript{13} for self-assessment of health related quality of life of patients with various chronic diseases, and a short form of a questionnaire of the International Association for Incontinence that is culturally adapted to Serbian context\textsuperscript{12}.

**Material and methods:**

*Study design and participants*

This prospective study was conducted at the Clinic of Urology, University Clinical Centre of Serbia in Belgrade in the period from December 2015 to August 2016. The sample size of study participants was calculated based on the formula for calculating the sample size for the error level $\alpha = 0.05$ and power of the study $1 - \beta = 0.8$. The required sample size to detect a statistically significant difference in LUTS and HRQoL was projected to 41 patients\textsuperscript{13}. The study includes 74 patients. All of them underwent endoscopic-transurethral prostatectomy (TURP) or classic-transvesical prostatectomy (PTV). Criteria for inclusion in the study were patients with informed consent, and a diagnosed subvesical obstruction due to BPH, previously treated pharmacologically (alpha blockers and 5-alpha reductase inhibitors), and age of 40 years and older. Criteria for exclusion from the study were: mental inability of the patient to fill out the questionnaire, depression (established by Beck’s Depression Scale the day before surgery) and patients who refused to participate in the study.

*Study instruments and variables*

The study included both subjective and objective approach for measurement of the outcomes of surgical treatment of HBP with regard to the LUTS and HRQoL. On admission to the Clinic, patients filled two questionnaires- Serbian version of ICS male SF questionnaire, and then the SF-36, a general questionnaire to assess the quality of life. After that they underwent ultrasound examination with measurement of prostate volume, residual urine and uroflowmetry. Patients with urinary catheter did not take an uroflow preoperative
testing (Q max – maximum flow rate), average flow rate and residual urine. For comparison with the original condition of the patient, the study protocol and clinical measurements were repeated 6 months after the date of the operation.

**Statistical analysis**

Data are presented as means ± standard deviations. Preoperative and postoperative values were compared using t test and Wilcoxon Signed Ranks Test. Correlation analysis was used to assess relationship between voiding and incontinence delta scores and quality of life delta scores. Delta score was calculated as difference between first and second measurement of examined variable. First measurement was obtained during hospital admission, and second measurement was obtained six months after surgery. All p values less than 0.05 were taken as values for rejection of the null hypothesis. All data were analyzed in SPSS 20.0 (IBM Corporation) software package.

**Results:**

**General characteristics of study participants**

Mean age of patients is 66.7±10.1 years. 37 (50%) patients had urinary catheter at hospital admission. All patients had prostate volume measured and average volume is 55.6±30.8ml. According to results in Table 1, significant decrease of voiding and incontinence symptoms is observed in all patients. Parallel, all dimensions of quality of life reveals significant increase of scores, except mental health. The highest change is observed in emotional health dimension.

Clinical parameters measured before and after surgery reveals objective improvement (Table 2). While Q max and flow rate reveals 2 and 6 times higher values, respectively, residual urine decreases six times.

The level of change of voiding and incontinence parameters correlates with levels of change of HRQoL parameters. According to results of correlation analysis, only significant correlation is between Role emotional change and voiding and incontinence change (Table 3). Other correlation coefficients that are near conventional significance level are between incontinence change and Bodily pain and Social function change. Since those coefficients are near conventional level of significance (0.05), they are taken in further consideration.
Discussion:

Benign prostatic hyperplasia and subsequent LUTS are very frequent pathology in the Europe region\(^1,5,1^4\), Global predictions are that by 2018, nearly 1.6 billion people will suffer from the symptoms of urine storage, and over 540 million people will suffer from symptoms of overactive bladder\(^2\). As is globally, aging of the population in Serbia is also contributing factor for the growth of incidence and prevalence. This study found that majority of patients with LUTS was in the seventh and eighth decade of life. BPH is a progressive disease and untreated enlargement of the prostate leads over time to LUTS and may be further complicated by acute or chronic infections. LUTS compromises everyday functionality, affects all HRQoL domains, causes numerous psycho-physical disorders\(^4\). An urgent condition in urology and one of the major complications and unambiguous sign of BPH disease progression is acute urinary retention (AUR)\(^1^5\). Progression of the disease is often not linear, and an acute detrusor decompensation of bladder may be the reason for the occurrence of AUR, and the other way is a chronic, weakening of the detrusor, RU accumulation and retention. Verhamme et al. state that in almost half of patients included in their study, AUR was the first reason for reporting to the urologist\(^1^6\).

The volume of the prostate as a risk for AUR occurrence and surgical treatment is the most studied entity. Studies affirm the assumption that patients with the prostate volume greater than 30 ml are in a higher risk of complications with BPH, or have progress to a stage when the surgical treatment becomes a modality of choice\(^1^7,1^8\). Measurement of residual urine in the bladder after urination is a common diagnostic procedure for patients with LUTS. Finding larger quantities of RU along with weak Qmax often is considered as a sufficient indication for surgical treatment\(^6\). Large quantities of RU, especially with hydronephrosis are an indication for the placement of a urinary catheter. Kolman et al. indicate that the patients with RU greater than 50 ml are in a high risk of developing AUR\(^1^9\). Mochtar et al. suggest that patients with RU larger than 300 ml are in the perspective likely candidates for surgical treatment\(^2^0\). RU values in the present study ranged from 40 to 300 ml. In the postoperative follow-up of treated patients in our study, similar to the study by Varkarakisa et al.\(^2^1\) a drastic reduction in the average values of residual urine occurs, almost as much as seven-times. Uroflowmetry is an essential part of the diagnostic algorithm, and despite all the constraints, uroflow is a significant indicator of urination disorders\(^1^8\). Crawford et al. find that the value of Qmax below 10 ml per second is in perspective a probable disease
progression. Uroflowmetry was done preoperatively for patients who had not a catheter and postoperatively for all patients. Preoperatively were recorded low values of Qmax, from 4 to a maximum of 14 ml / s. Postoperatively was determined a drastic increase in Qmax. This finding is similar to the findings of the study by Varkarakisa et al., or Hakenberg et al. as well as the meta-analysis of Wook Lee, who agree that surgical treatment of BPH among other things leads to an increase in Qmax. When conservative treatment does not produce satisfactory results, surgical treatment is becoming the treatment of choice. TURP is the gold standard in the treatment of BPH, but for prostate of greater volume PTV is the method of choice. In the United States, this operation is applied to only 3% of patients surgically treated for BPH. In our study, 23% of patients underwent transvesical prostatectomy. There is a generalized belief that this traditional, open surgical technique is represented only in the economically less developed countries, however, studies suggest a somewhat greater representation of these operations, so that in Sweden almost 12% of the patients are operated on by this technique, and 14% in France, and some studies suggest an even larger share of PTV of the total number of the operated, so Serrette in the Italian study states that 32% of the total number were subjected to PTV, and 40% in the study by Moses et al. conducted in Israel.

Subsequently was analyzed the change of summary scores of voiding and incontinences on discharge and 6 months after the date of surgery. The values obtained before and after surgery were significantly different in terms of reduction of voiding scores during the second measurement. These results are complementary with the results of different studies dealing with similar comparative analysis of pre- and post-operative treatment both for TURP and PTV. The intervention drastically reduces the detrimental impact of voiding on the quality of life of all patients and this finding is consistent to other studies. Namely, a large number of patients who prior surgery has a deteriorated quality of life due to frequent voiding after surgery report "it does not affect" or "little".

Physical Function (PF) is one of the domains of quality of life of SF 36 scale affected by LUTS. Incontinence rather than voidance significantly reduces the physical function. Slight, but statistically significant increase was determined of the score of physical function six months after the surgery. Engstrom et al. report that difficulties related to urination, especially waiting for the voiding, straining during voiding and incomplete emptying of the bladder decrease physical score. In our study, surgical treatment statistically significant increased the ability of patient’s physical role, by 20% approximately. According to
Speakman et al. the quality of overall health is affected by symptoms of LUTS though in significantly. Our study found a little but statistically significant improvement of the overall health score, and of vitality six months after the treatment.

According to the available literature the social function (SF) score is most deteriorated by incontinence, and particularly among elderly patients. In our study, surgical treatment yields an evident, statistically significant improvement in the score of the social function. Welch et al. in his study shows that LUTS significantly and negatively affect the emotional role (RE) from diseases such as gout, hypertension, angina pectoris, and diabetes mellitus. Our testing shows that surgical treatment leads to a statistically significant improvement in this score. The impact of LUTS on mental health (MH) is one of many variables that we examined. Hunter et al. state that LUTS affect mental health significantly more negatively than back pain, varicose veins or ulcers. In our study, only patients of good or satisfactory mental status were included, since all patients with a score over 20 at Beck depression test were excluded from the study. That may explain why differences in average mental health values before and after the surgery in our study are small, and statistically in significant. However, a comparative analysis of the total physical and mental scores before and after surgery undoubtedly indicates a their significant increases after surgery, which supports the justification and appropriateness of the operative treatment to solve LUTS caused by BHP.

Welch et al. emphasize the impact of surgical treatment to the following domains: physical role, vitality, emotional role, the total physical score, physical functioning, bodily pain, social functioning and mental health. At the same time, they indicate a deterioration of HRQoL that is directly proportional to deterioration of LUTS. Welch, Hunter et al. and Engstrom et al. recognize LUTS and especially incontinence, disturbs most of the domains of quality of life. The total score of quality of life has significantly higher value after the intervention compared to the value before the intervention. Decreased total score of quality of life caused by severe LUTS is also present in the study by Quek et al., a study by Haltbakk, which especially emphasizes the population of advanced age but also in a population study conducted in Serbia. Meta analysis of Ahyai et al. shows that TURP reduce IPSS QoL score (p > 0.3), similar as to bipolar TURP and the HoLEP laser’s resection of the prostate. Varkarakis et al. show the chronology of statistically significant improvement in IPSS QoL score after the PTV, in the immediate postoperative period, then 8 and 12 months after surgery.
This is a pioneer study in Serbia, which assesses the effects of operative treatment of BPH, on LUTS and HRQoL by application of new system-score instruments, but it has some limitations. Although sample was representative to detect statistical significant results, study findings are specific for Serbian patients and should not be widely generalised prior verifying in a larger sample. In addition, it represents the work results of one clinic, which is the tertiary level and university based inpatient care facility, therefore service differences should be considered in a comparative analysis. Though both system-score instruments, the SF-36 questionnaire and ICP-male, are standardised questionnaires and culturally adapted, they are self-administered and may contain a portion of under or overestimation of some aspects of quality of life and LUTS due to patients cognitive abilities such as memory, or willingness to report private issues. Finally, this study shows results of six months follow-up after surgery, that is a short-term effects rather than impact assessment which requires recording 12 months and more after the surgical treatment.

Conclusions
After surgery, almost all dimensions of quality of life keep changing significantly towards greater score, which clearly suggests the positive impact of the intervention on patient’s quality of life, including very large (e.g. emotional role) and small (e.g. overall health) improvements. After BPH surgery, patients will likely have normal voiding symptoms, almost annulated involuntary control over voiding and better all dimensions of HRQoL.

The surgical treatment of BPH either as classic and endoscopic surgery, leads to the improvement of objective clinical parameters, to the release from the catheter, as well as to reduction of residual urine, and increase in Qmax. The operation significantly reduces the subjective parameters in voiding symptom score and incontinence measured by the ICS male SF questionnaire, in contrast to most famous IPSS score, this approach precisely measure difficulties in voiding and incontinence, and is a reliable diagnostic tool highly recommended for complementary measurement of subjective and objective parameters of LUTS and HRQoL prior and after the treatment of BPH.


13. **Cronbach LJ.** Coefficient alpha and the internal structure of tests. Psychometrika [Internet].1951;16(3):297–334. Available from: http://dx.doi.org/10.1007/BF02310555


Table 1. New system-score measurements of LUTS and HRQoL: ICS-male SF and SF-36 results before and after the surgery of BOH, n=75

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>After surgery</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICS-male SF</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voiding</td>
<td>13.49±3.30</td>
<td>1.50±1.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incontinence</td>
<td>5.74±3.97</td>
<td>0.57±0.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>SF-36</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td>60.34±27.11</td>
<td>66.92±24.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Role Physical</td>
<td>44.18±40.07</td>
<td>61.30±31.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body pain</td>
<td>47.64±26.46</td>
<td>60.73±22.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Global health</td>
<td>42.78±15.72</td>
<td>45.37±14.28</td>
<td>0.008</td>
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<tr>
<td>Vitality</td>
<td>51.64±10.99</td>
<td>57.12±11.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social function</td>
<td>49.88±21.01</td>
<td>62.53±18.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emotional</td>
<td>29.64±36.27</td>
<td>65.36±34.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mental health</td>
<td>53.59±6.76</td>
<td>52.82±6.32</td>
<td>0.305</td>
</tr>
</tbody>
</table>

*Pearson correlation analysis
Table 2. Clinical parameters used for evaluation of surgical procedure

<table>
<thead>
<tr>
<th>Clinical Parameters</th>
<th>Before surgical procedure</th>
<th>After surgical procedure</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q max</td>
<td>8.82±3.05</td>
<td>22.76±4.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average flow rate</td>
<td>4.21±1.59</td>
<td>10.55±3.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residual urine</td>
<td>87.50±44.47</td>
<td>12.63±18.69</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Pearson correlation analysis

Table 3. Correlation of voiding and incontinence scores changes and HRQoL score changes, n=75

<table>
<thead>
<tr>
<th>Delta Voiding</th>
<th>Delta Incontinence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation</td>
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<tr>
<td></td>
<td>Coefficient.</td>
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<tr>
<td>ΔPF</td>
<td>0.027</td>
</tr>
<tr>
<td>ΔRP</td>
<td>-0.049</td>
</tr>
<tr>
<td>ΔBP</td>
<td>-0.197</td>
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<tr>
<td>ΔGH</td>
<td>-0.187</td>
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<tr>
<td>ΔVit</td>
<td>-0.149</td>
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<tr>
<td>ΔSF</td>
<td>-0.145</td>
</tr>
<tr>
<td>ΔRE</td>
<td>-0.229</td>
</tr>
<tr>
<td>ΔMH</td>
<td>-0.057</td>
</tr>
</tbody>
</table>

*Pearson correlation analysis

Received on February 27, 2017.
Revised on April 17, 2017.
Accepted on April 20, 2017.
Online First April, 2017.