

Green Light Photo Selective Vaporization of the Prostate vs. Transurethral Resection of Prostate for Benign Prostatic Hyperplasia

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Abstract:

Introduction: Green light photo selective vaporization of the prostate (PVP) is a minimally invasive method of treatment for clinical benign prostatic hyperplasia with fewer side effects. The aim of this study is to evaluate the safety, effectiveness and cost analysis of PVP compared with transurethral resection of prostate.

Methods: A systematic search was done in Cochrane, TRIP database, MEDLINE, NHS EED, NIHR HTA, CRD, Health star database, Pro Quest, Psycinfo and Google Scholar to find randomized control trials, systematic reviews and HTA reports. The searched keywords were Green light laser (PVP or KTP) and prostate. The cost analysis was done by the perspective of society and providers.

Results: Complication rate in 12 included evidences ranged from 0-9.3%. The complication rate of TUR-P (Transurethral Resection of Prostate) was more than PVP. Changing in flow rate reducing residual urine, improving patients' symptoms and QOL (Quality of life), and operative outcome length of operation varied from no significant to significant differences in favor of TURP. Unit cost in both social and provider view was significantly high in PVP in comparison with TURP. Increasing the number of patients did not change the cost analysis.

Conclusion: PVP is a safe method for treatment of clinical BPH, but there is a lack of evidence for the evaluation of effectiveness. Overall, the unit cost for PVP was significantly more than TURP; for this reason this method could not be conducted in very wide indications, because of high cost.

Keyword: laser vaporization; ablation techniques; health technology assessment; benign prostatic hyperplasia.

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Introduction

Benign prostatic hyperplasia (BPH) is the most

common condition affecting aging men. The prevalence of BPH is reported to range from 1.2% in men 40–49 to 36% in those >70 years in an

Iranian population study (1). Treatment includes watchful waiting, medical management and surgical interventions. The lifetime risk of requiring a surgical intervention has been estimated to be about 29%. Transurethral resection of prostate (TURP), is considered as the gold standard surgical method of treatment for BPH. The TURP method requires 2-4 days of hospital stay. Since using laser technology in benign prostatic surgery reduces bleeding and the period of hospital stay; thus, patients and providers of health services tend to increasingly use these technologies. But, there is an ever arising question that “does information provided on the catalogues of manufacturing companies about the efficacy, effectiveness, and safety outweigh the cost of using these technologies?” This study addresses this issue and conducts a cost-effectiveness analysis of benign prostatic enlargement treatment using current approach (TURP) in comparison with green light laser methods.

Green light photo selective vaporization of the prostate (PVP) is a new minimally invasive method which has recently been introduced for the treatment of BPH. This method seems to have potentially lower complication rates than TURP which is considered the “gold standard” of surgical interventions. This is a surgical technique that uses laser to vaporize prostate tissue with minimal damage to other tissues. PVP evolved laser techniques from coagulation to vaporization. In the new generation of green light laser, the energy level increases from 80w to 120w and a lithium triborate (LBO) crystal is inserted in place of Potassium Titanyl Phosphate KTiOPO_4 (KTP). The special characteristic of green light laser is resorption of hemoglobin which is critical for patients with uncontrolled coagulopathy, or on the anticoagulant agents. It seems that learning curve of green light is much less than Holmium yttrium aluminium garnet (YAG) laser (2).

The attractiveness of modern technologies both for patients, who are seeking for high quality and effective services, and health care providers, who are being threatened by their opponents in the health care market, has made governments to take measures in order to reach a balance between high effectiveness and high costs of modern technologies. Therefore, governments have been compelled to adopt appropriate decisions considering ethical issues and fairness as a principal factor in the

process of decision making. Islamic Republic of Iran has been considered as a country on early stages of development. The country's limited production capability has made it as a big importer in medical device industries. Imports account for an estimated 97.7% of the market, despite the manufacture of basic consumable items such as syringes, needles and catheters, dental instruments and fittings and orthopedic appliances (3). The majority of medical equipment is being imported without any Health Technology Assessment studies, or restriction on them. Consequently, it has brought about some troubles such as rapidly growing currency outflow, high dependence on foreign technologies, and high rate of unemployment due to the replacement of capital intensive equipment with labor intensive equipment (Imports were valued at US\$591.7 million in 2009, with Germany and the Netherlands being the leading suppliers) (3-4).

Method

Search strategy: The last search was in February 2009. The publication date was limited from 2000 to February 2009. Cochrane, TRIP database, MEDLINE via Pubmed (including Clinical Queries), NHS Economic Evaluation Database, NIHR HTA, NHS Centre for Reviews and Dissemination (CRD), Health star database, Dissertation Abstracts Online (UMI) via ProQuest, Psycinfo and Google Scholar were the databases searched and reviewed. EMRO-WHO website and websites of Iranian Ministry of Health were also searched for epidemiological and economic studies in Iran.

The search strategy was: Green light laser (PVP or KTP) AND prostate. “Laser vaporization” (as selected MeSH term) and “Prostate” were the keywords we searched in Pubmed (including Clinical Queries). We limited the search to Meta-analysis and Randomized Control Trial studies as well as “Title /abstract” field. In Cochrane Library database we searched for keywords in “Title, abstract and keyword” fields. We searched Google Scholar for “Laser Coagulation” or “green light laser”, “Prostate” and “Health Technology Assessment” in “Medicine, Pharmacology, and Veterinary Science” subject area. In other databases, we searched for the above keywords as well. Both 80W KTP PVP and 120W LBO PVP were included in this report.

Two independent reviewers studied the selected studies. A critical appraisal was done by Critical Appraisal Skills Program (CASP) International Tool. For any disagreements, a third party was invited to solve the problem.

The cost-effectiveness analysis was considered as a principal method in this study. In order to take patients' preferences into account, the data related to patient's quality of life were gathered. The data were used to compare the outcome of the interventions. Identification and analyses of costs and outcomes were taken from the perspectives of society and providers (5). Data related to effectiveness were obtained from the secondary data using systematic reviews. Standard costing method was used to calculate incurred costs for each alternative. All activities for each treatment intervention were identified through focus group discussion and current guidelines. Five cost items were categorized (staff, equipment, buildings, consumables, and utilities). The straight line method of depreciation (the difference between purchasers' value and scrap value divided by the useful life) was used for estimation of equipment

costs. Since there were some uncertainties for some variables, and to increase the generalizability of results, sensitivity analysis was done (6).

Cost Analysis in health; a Practical Approach: Data analysis was done via Microsoft Excel 2007. Since all costs and outcomes were related to one year, there was not need to discount the values. Whereas the overhead costs were similar for both alternatives, these types of costs were not considered in the analysis (7).

Results

A total of 14 articles were identified, 6 of which were excluded based on their titles and abstracts. Eight articles remained according to the inclusion and exclusion criteria. Systematic reviews and RCTs were evaluated through CASP international worksheet. The remaining articles were evaluated by expert evaluators and professional librarians. Eventually, five articles were selected to be reviewed as shown in Figure 1.

Only five clinical trials were found for green light laser, just one of which was RCT. But the

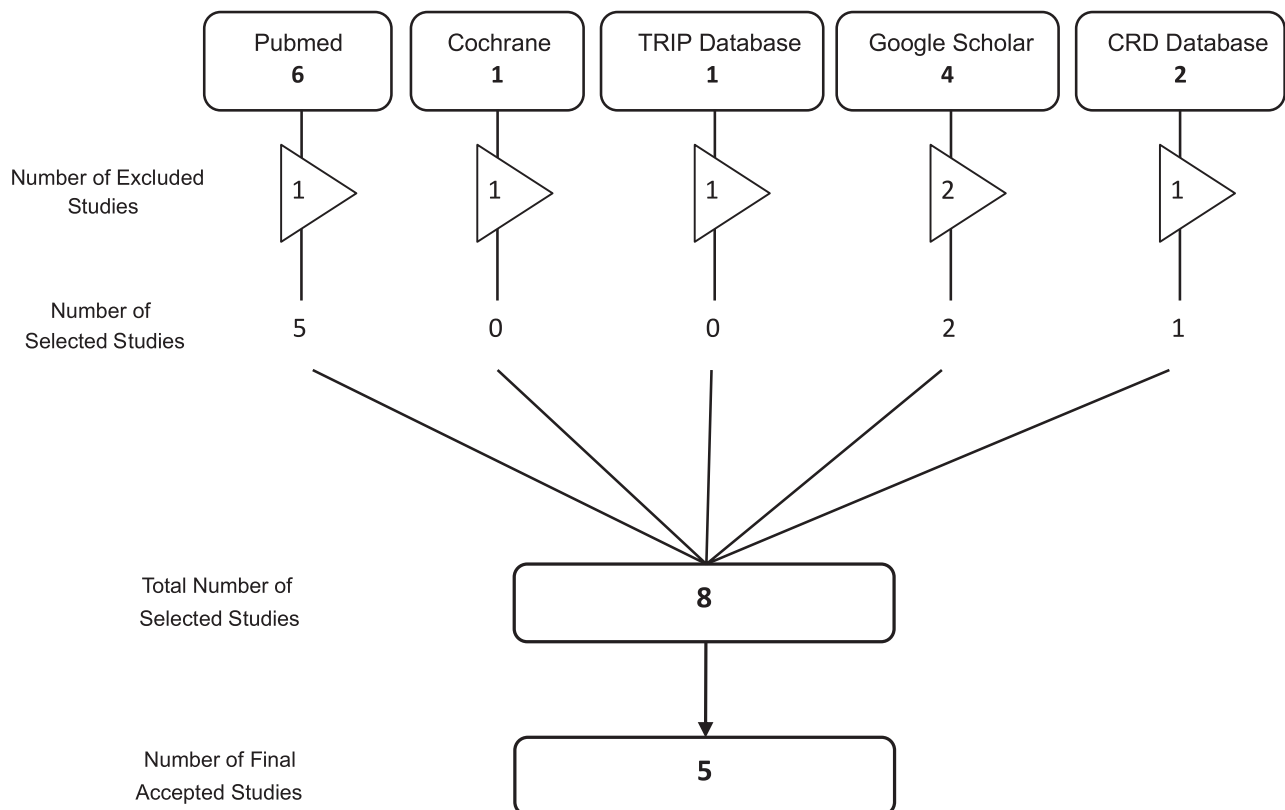


Figure 1. Study selection flow chart.

multicenter international green light cohort was used for the monitoring the morbidities. A critical appraisal was done for all five articles by using CASP International Appraisal Tool. In these five trials overall 641 patients with clinical benign prostatic hyperplasia are compared in two groups between green light in one arm and TUR-P, and open prostatectomy in other arm. All studies used at least International Prostate Symptom Score (IPSS) questionnaire for symptom scoring pre- and post- surgical acts as a subjective tool and QMax, and post void residual urine (PVR) as objective outcome measurement.

Only one Australian study had been designed as Randomized Control Trial (RCT) to compare green light with TUR-P (9). In four of the five selected RCTs, green light laser was compared by TUR-P, and just in one of the studies open prostatectomy

was the control. The baseliner characteristics were almost comparable in all studies, and the follow-up time was from 3 to 18 months. Table 1 shows comparison of results in five studies.

Safety and Effectiveness

Safety

Table 1 showed that no intraoperative complication reported in the five studies for KTP PVP. Intraoperative complications in TURP patients including the need for transfusion ($P=0.001$), capsule perforation ($P=0.001$) or TUR syndrome was significantly more than the KTP PVP groups (10).

Pooled complication rates from the 12 included case series included in the SR, ranged from 0%

Table 1. Results of selected articles in point of safety and effectiveness

Study	Comparison	Participants		Age (mean)		QMax		PVR		IPSS		Transfusion	
		PVP	Control	PVP	Control	PVP	Control	PVP	Control	PVP	Control	PVP	Control
Horasanli K, et al. (8)	TUR-P	39	37	69.2	68.3	13.3±6.9	20.7±11.3	NR	NR	13.1±5.8	6.4±7.9	0	3(8%)
Bouchier-Hayes DM, et al. (9)	TUR-P	38	38	65.23	66.23	11.96±8.23	8.56±9.08*	27	37	14±9.8**	12.9±10.6	0	1
Ruszat R, et al. (10)	TUR-P	269	127	72	68	14-20	18-24	NR	NR	Less than 8 (In 24 mo)	Less than 8 (In 24 mo)	0%	7(5.5%)
Alivizatos G, et al. (12)	Open Prostatectomy	65	60	74	67.5	16	15.1	17	12	9(12 mo)	8(12mo)	0	8(13.3%)
Skolarikos A (13)	TUR-P	80	75	NR	NR	15.42±3.68	18.3±5.78	26.97	50.41	9.32±4	10±2.8	0	5

Study	TUR Syndrome		Urinary Retention		Incontinence		Duration of Hospitalization (days)		Length of Operation		Reoperation		Stricture	
	PVP	Control	PVP	Control	PVP	Control	PVP	Control	PVP	Control	PVP	Control	PVP	Control
Horasanli K, et al. (8)	0	0	6(15.3%)	0	0	0	1.7±0.8	4.8±1.2	87±18	51±17	7(7.9%)	0	2(5.1%)	3(8.1%)
Bouchier-Hayes DM, et al. (9)	0	1	3	3	NR	NR	1.08	3.4	12.2±8.6	44.52±30.23	2	0	5	8
Ruszat R, et al. (10)	0	2(1.6%)	27(34%)	9(16%)	NR	NR	3	4.7	72	53	18(6.7%)	5(3.9%)	12(4.5%)	4(3.1%)
Alivizatos G, et al. (12)	0	-	5(7.69%)	10(16.67%)*	0	0	2	6	80	50	3(4.6%)	3(5%)	2	1
Skolarikos A (13)	NR	NR	NR	NR	NR	NR	2	4	61.32	43	NR	NR	NR	NR

*Increasing in fellow

**Decreasing in IPSS

***Recatheterization

for bladder stenosis to 9.3% for mild-to-moderate dysuria. Compared with TURP, PVP complication rates were either similar, or considerably lower, particularly urinary retention and clot retention. Stafinski et al. reported analyses of relative risk of a complication for these two methods of surgery (11). Intraoperative complications were comparable between the PVP and TURP groups except for clot retention which was significantly less in PVP. It seems the safety of PVP was accepted by authors.

Effectiveness

Primary and secondary outcomes for efficacy included: changing in flow rate, reducing residual urine, improving patients' symptom scores-- quality of life, operative outcomes, length of surgery, and staying in the hospital.

According to the illustrations of RCTs in Table-1, the difference of postoperative IPSS and QMAX between PVP and TURP varied from no significant difference(9,11,12,13) to significant difference in favor of TURP (8,10). On the other hand, IPSS, IPSS Quality of Life (QoL), and Qmax had a comparable improvement for patients undergoing either PVP, or open prostatectomy (12). Reoperation rates in the studies were reported to be between 0% and 7.5% for PVP patients (8-13). However, learning curve of surgeon as a possible reason should be noticed.

After identification and valuing the used resources in the different stages of each intervention, the unit cost for a surgery using standard costing method was obtained. The valuation of physician's visits and services which were delivered at the hospital were based on the governmental tariffs. Medical equipment and consumables values were based on the market prices. There was a similarity in building and overhead costs for both alternatives; therefore,

Table 2. Unit cost for different surgical methods (300 patients)

	Surgical Method			
	Transurethral Resection		Green Light	
	Study Perspective		Study Perspective	
	Societal	Provider	Societal	Provider
Unit Cost	4298016	2428016	8831875	7896875
The Incremental Cost in Comparison with the Current Method	0	0	4533858	5468858

Table 3. Unit cost for different surgical methods (200 patients)

	Surgical method			
	Transurethral Resection		Green Light	
	Study perspective		Study perspective	
	societal	provider	societal	Provider
Unit cost	4325794	2455794	9171875	8236875
The incremental cost in comparison with the current method	0	0	4846080	5781080

these items were not entered in the analysis. In addition to societal perspective, costing was done from the perspective of providers, where costs such as patients' and their families' time off costs will not be included in the analysis. Increasing the number of delivered services reduces the unit cost and this will influence the cost-effectiveness, thereby the number of patients was considered as an important variable. Tables 2 and 3 represent unit cost of two alternatives for 300 and 200 patients, and also from societal and providers' perspectives.

Sensitivity Analysis

As the number of surgeries increases, the average cost of delivering a service decreases. The one way sensitivity analysis showed that this set was not cost-effective in the range of 200 to 300 patients. In order to examine the threshold level of uncertain variable, the number of patients increased to 2500 (as an optimistic level of demand), but the results did not change. It means that decreasing the amount of unit cost because of increasing in the number of surgeries could not make the new technologies cost-effective.

Discussion

In terms of safety, KTP PVP seems to have similar intraoperative complication rates compared with TURP, or Open prostatectomy (8-13).

In terms of efficacy, functional outcomes including Qmax, PVR, IPSS and QoL were similar in three of the five RCTs that compared PVP with TURP or open prostatectomy (9, 12-13). In the remaining studies, functional outcomes were in favor of TURP compared with PVP (8, 10). Pooling data showed operation time in PVP was more than TURP in which the learning curves of

urologists may explain this difference.

However, duration of hospital stay in all of the studies was in favor of PVP.

Although the results of studies led the surgeons to a safe and effective approach, some critical appraisal issues should be discussed in this part. Population and eligibility criteria of the studies were variable and heterogeneity of data made it impossible to conduct any Meta-analysis. Randomization and blinding methods is unclear or has not been performed at all. On the other hand, no long term follow up has been reported, and follow up in current studies was not similar. However, the main advantage of PVP can be its safety for patients with coagulopathy or high risk patients on anticoagulant. Unfortunately, the prevalence of coronary arterial diseases in Iran is 18-22.5% which is age related and may include a significant problem of old men with clinical BPH. This population will need a safe and effective option for TURP.

The results of RCTs showed that there are slight differences in the effectiveness of new technologies. Thus, considering the differences in unit costs between new alternatives and TURP, it is clear that the current method of prostatic surgery will remain as a dominant method. Meanwhile reduced bleeding and the period of staying at hospital can induce patients and providers to use the new technologies. But it has to mention that Green Light Laser set is more expensive than TURP and even other laser method like as Holmium and Thulium according authors' pervious study (15).

Conclusion

Overall, KTP PVP seems to be safe and almost effective as TURP for the treatment of clinical BPH. More well-designed multi-centric RCTs are required to confirm their effectiveness and long term outcomes. In term of cost analysis the PVP does not have a reasonable cost value even if it is compared with Holmium laser enucleating of the prostate (HOLEP). But limited application of KTP PVP still can be a good option for patients with high cardiovascular risk.

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