

Long-term outcome of Trans Urethral Prostatectomy in benign prostatic hyperplasia patients with and without diabetes mellitus

Mohammad Soleimani, Seyed Yousef Hoseini, Majid Aliasgari, Farid Dadkhah, Alireza Lashay, Erfan Amini
Urology and Nephrology Research Center (UNRC), Shahid Modarress Medical Center, Shahid Beheshti University, M.C. (SBMU), Tehran, I.R. Iran.

Abstract

Objective: To compare the different aspects of the postoperative outcomes in diabetics and nondiabetics of transurethral prostatectomy in patients with benign prostatic hyperplasia.

Methods: From December 2000 to December 2003, a total of 138 men with BPH, who were candidates for transurethral resection of the prostate (TURP), were selected for this study, of these 20 were diabetics. The International Prostate Symptom Score (I-PSS) and the erectile function were assessed preoperatively and during an average follow-up period of 63 months postoperatively. Comorbid conditions and all surgical complications during the follow-up were recorded.

Results: No significant differences were detected between the baseline IPSS and the prostate volume in diabetic and nondiabetic patients. Both groups showed significant reductions in IPSS, and greater reductions were detected in nondiabetic patients 6 months after their operations that were not statistically significant (23.5 ± 8.0 versus 20.9 ± 7.6 respectively, $p = 0.169$). There were no significant differences in the perioperative complications. The incidence of a second TURP was higher in diabetics (25% vs. 7.8%, $p = 0.033$). Although not statistically significant, a higher incidence of postoperative erectile dysfunction (ED) in diabetic patients (37.5% vs. 11.5%, $p = 0.073$) was observed.

Conclusion: TURP is a beneficial and safe procedure in diabetic patients with BPH and is not associated with a higher incidence of perioperative or postoperative complications except for the possible postoperative ED and the retreatment rate that seems to be higher (JPMA 60:109; 2010).

Introduction

Diabetes mellitus and BPH increase in prevalence with age in agreement.¹ At the age of 60 approximately 60% of men are affected with some degrees of clinical BPH.² The prevalence of DM has been estimated to be 21.6% for those above 65 years of age in USA.³

Therefore, it could be expected that a major fraction of the patients with BPH concomitantly suffer from diabetes and vice versa. In addition, it has been demonstrated that diabetes is associated with greater BPH symptoms severity even after an age adjustment.⁴ Longstanding diabetes can cause bladder dysfunction and may also cause faster annual growth rate of the prostate and affect bladder outlet resistance.^{5,6} If lower urinary tract symptoms in diabetic patients with BPH are partly due to diabetes, it becomes relevant to know if these patients respond to the treatment in the same way as the

nondiabetic patients. This prospective study was undertaken to compare the different aspects of the postoperative outcomes of TURP, in diabetic and non-diabetic patients.

Patients and Methods

From December 2000 to December 2003, a total of 138 men with benign prostatic hyperplasia and severe lower urinary tract symptoms, who were candidates for a surgical therapy were included in the study. The group was divided into two subgroups; the first one included patients defined as diabetics with a fasting blood glucose level of more than 126 mg/dl, while the second group comprised of patients without diabetes mellitus. Patients with prostate cancer or a history of previous prostate surgery were excluded from the study as well as men with neurogenic bladder dysfunction or urethral stenosis.

UNRC has adopted codes of ethics considering ethical

issues on human experimentations. All patients completed the informed consent prior to investigations.

At the first examination, a complete medical history was elicited by a standardized interview. All patients were evaluated by a cardiologist in order to determine the preoperative cardiac risk using American Heart Association guidelines.⁷ Urodynamic testing was performed to exclude incompatible patients if indicated. Other data including sonographically determined prostate volume, operative time, transfusion rate, length of admission, postoperative outcomes, and complications were compared between the diabetic and the nondiabetic patients.

Using the abridged 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for evaluating the erectile dysfunction, the patients were classified into two categories based on the scores: moderate to severe erectile dysfunction (IIEF-5 score 5 to 16) and mild or no erectile dysfunction (IIEF-5 score 17 to 25). Lower urinary tract symptoms were evaluated using the International Prostatic Symptom Score (IPSS), also the quality of life according to the urinary symptoms. IPSS, the quality of life in line with the urinary symptoms, and the erectile function were assessed during the follow-up period and were compared in the early and late postoperative follow-ups. Data collected 6 months after the surgery, were considered as the "early" postoperative outcome, and the patient's condition at the latest visit (the end of follow-up) as the "late" postoperative outcome. (The duration of the follow-up period was up to 80 months with a mean duration of 63 ± 27.7 months). In addition, during the follow-up period, patients suffering from moderate to severe urinary postoperative symptoms were evaluated for urethral stenosis, bladder neck contracture or regrowth of prostatic adenoma.

All collected data were analyzed using SPSS for windows version 12 (SPSS Inc, Chicago, IL)

Results

A total of 138 Subjects were included in this study during the specified period, 20 (14.5%) of them were diabetics aged between 52 and 85 years old with the mean age of 70.3 ± 6.6 .

Except for the higher prevalence of hypertension and the erectile dysfunction in diabetic patients, no significant differences were noted in the preoperative data including age, sonographically determined prostatic volume, renal function and cardiac risk between the two groups. No significant differences were noted between the two groups with respect to the perioperative data such as the operative time, transfusion rates and perioperative complications including myocardial infarction, gastrointestinal bleeding, wound infection, acute tubular necrosis and the length of admission. Perioperative mortality occurred only in one nondiabetic patient. The

baseline and perioperative characteristics of these groups have been compared in Table-1.

The improvement in both groups was statistically significant for the IPSS at the early and the late follow-ups against the baseline values ($P < 0.05$). The mean \pm SD IPSS decreased from 27.0 ± 6.6 to 6.0 ± 2.7 and 10.3 ± 7.4 after the surgery in diabetic patients, and from 27.9 ± 6.6 to 4.4 ± 5.6 and 6.5 ± 7.7 in nondiabetic patients, at early and late follow-ups after surgery, respectively.

Although statistically insignificant, a greater reduction of IPSS was detected in nondiabetics compared with diabetics six months after the surgery (23.5 ± 8.0 versus 20.9 ± 7.6 respectively, $p = 0.169$).

The mean IPSS values and the quality of life in relation to the urinary symptoms six months after the operation, and on the last follow-up in both groups are presented in the Table-2.

The incidence of the postoperative ED was evaluated among the patients with pre-operative normal erectile functions. Of the diabetics 37.5% and 11.5% of nondiabetics with mild or no preoperative erectile dysfunction were found to have moderate to severe ED six months after the surgery; accordingly. Furthermore, the incidence of the postoperative ED was higher but not statistically significant in the diabetics ($p = 0.073$).

Among the 20 diabetics treated by TURP, 5 patients (25.0%) required a second TURP during their follow-ups, while a reTURP was performed for 9 (7.8%) of 107 non-

Table-1: The baseline and the perioperative data of the patients with and without coincidental diabetes.

	Non-Diabetics	Diabetics	P-Value
Age (yr)	69.9 \pm 6.8	72.1 \pm 4.1	0.178
Prostate volume(ml)	47.1 \pm 13.6	47.7 \pm 15.5	0.871
Baseline IPSS*	27.9 \pm 6.6	26.9 \pm 6.6	0.551
Prevalence of hypertension	18.6%	40.0%	<0.037
Prevalence of preoperative ED+	18.6%	60.0%	<0.0001
Mean operative time (min)	45.6 \pm 14.0	40.5 \pm 18.5	0.156
Transfusion rate (number of packed cells)	0.085 \pm 0.33	0.2 \pm 0.6	0.220
The Mean length of admission (day)	2.6 \pm 0.9	3.0 \pm 0.9	0.068

*IPSS: International Prostatic Symptom Score
+ED: Erectile Dysfunction.

Table-2: A comparison between the early and the late postoperative outcomes in both the diabetics and the nondiabetics during their follow-ups.

	Non-Diabetics	Diabetics	P-Value
IPSS at 6m follow up	4.4 \pm 5.6 (n=117)	6.0 \pm 2.7(n=20)	0.211
QOL* at 6m follow up	0.55 \pm 1.3 (n=117)	0.6 \pm 0.9(n=20)	0.829
IPSS at the latest follow up	6.5 \pm 7.7 (n=89)	10.3 \pm 7.4 (n=18)	0.06
QOL at the latest follow up	1.1 \pm 2.2 (n=89)	2.4 \pm 2.4 (n=18)	0.027

QOL*: Quality Of Life.

diabetics treated by TURP ($P=0.033$). In addition to the higher incidence of reTURP in diabetics, a shorter interval between the two operations was noted in the diabetic group (31.4 ± 10.1 m vs. 50.1 ± 12.9 , $p=0.029$). The mean \pm SD IPSS decreased from 24.2 ± 9.2 to 4.2 ± 1.6 after surgery in 9 non-diabetics ($P < 0.0001$) and from 21.4 ± 2.2 to 5.6 ± 0.5 in 5 diabetic cases ($P < 0.0001$) who required a second TURP.

Discussion

A possible relationship between diabetes and BPH has been discussed in different studies but it is unclear if diabetes might affect the therapeutic benefits of the surgery in BPH patients. Therefore, we conducted a prospective study with long term follow up to compare the different aspects of postoperative outcomes and complications in the diabetics and nondiabetics.

The prevalence of diabetes in BPH patients who are candidates for surgery varies from 5% to 17% in different studies,^{8,9} and it was 14.5% in our study.

It has been reported that diabetics have significantly greater BPH severity of symptoms when compared with the healthy controls⁴ and demonstrate a significantly faster annual prostatic growth rate.⁵ This association between diabetes and the severity of the BPH symptoms could be explained by various mechanisms. Longstanding diabetes can cause bladder dysfunction, which involves an autonomic neuropathy leading to functional parasympathetic and possibly sympathetic denervations of the detrusor.^{10,11} Atherosclerosis-induced ischaemia may affect detrusor function and result in fibrosis, smooth muscle atrophy and bladder non-compliance.¹² Diabetes can affect dynamic and static components of the bladder by impairing detrusor function and increasing the prostatic growth rates, respectively.^{13,16} Diabetes and hyperinsulinaemia result in reduced NOS/NO in the prostate and bladder, leading to muscle cell proliferation and structural changes in the prostate and simultaneous increased contraction which affects outlet resistance and bladder compliance.¹⁷

Despite this association, we were unable to show any differences in the baseline IPSS, comparing the diabetics and the nondiabetics. A possible explanation could arise from the fact that in our study, all patients were subjected to surgery and severe lower urinary tract symptoms were recorded in the majority of patients including the diabetics and nondiabetics. Other studies that have shown a relationship between diabetes and the severity of symptoms in BPH which comprised of patients with mild to severe urinary symptoms. In addition, no differences were detected in the mean prostate volume of the diabetics and the nondiabetics in this study. According to different studies, higher prostatic growth rate in diabetic patients may be related to the long-term exposure of the prostate stroma to the increased growth factor levels as a result

of chronic hypoxia.^{13,14} Some studies though indicating a decreased perfusion of the transitional zone of the prostate have proved no differences in the mean prostate volume between diabetic and nondiabetic BPH patients.¹⁵ Berger et al have shown a greater volume of the prostate in diabetics, however, in their study the average age of the diabetics was approximately 20 years higher than those of the nondiabetics and the difference between the mean prostate volumes may be age-related.¹⁶

In support of this claim, Bruke et al. showed diabetes was not significantly associated with the annual percentage of changes in the prostate volume or the serum PSA level in a group of 2115 white men aged 40 to 79 years, however, a significant association was observed between the progression of the symptom severity and the decline in Qmax over the time.⁶ Therefore, these data suggest that the presence of diabetes may be less directly linked with the prostate growth and more closely related to the dynamic components of the lower urinary tract function.

In this study patients were selected for surgery according to their urinary symptoms and urodynamic study was not performed routinely in all diabetic patients. Although urinary symptoms of diabetic neuropathy are similar to those of BPH and we did not confirm the presence of obstruction by pressure flow study, considerable decline in IPSS after surgery in our diabetic patients shows that a significant obstructive component was present and they were appropriately selected for surgery therefore the beneficial outcomes of surgery in these patients was not affected by detrusor dysfunction due to the longstanding diabetes.

Despite the more frequent occurrence of the perioperative complications in most of the surgical interventions in diabetics,¹⁸ Ibrahim et al revealed no higher coinciding mortality or morbidity in diabetics except for the postoperative bacteriuria which was more frequent in diabetics.¹⁹ In our study, the incidence of the perioperative complications was not higher among the diabetics.

According to the previous studies, the chance of undergoing a second procedure has been reported ranging from 0.5% to 7% and 2.8% to 16.8% for an open prostatectomy and TURP, respectively.²⁰⁻²² We noticed a higher retreatment rate in those diabetic patients who underwent TURP in our study (25% vs. 7.8%, $p=0.033$). A possible explanation for this higher incidence of reTURP in diabetics may be the faster growth rate of the prostate in such patients because of the tissue hypoxaemia. In addition, an impaired detrusor function in diabetics results in a lower maximum flow rate for any given level of the bladder outlet resistance, and therefore, the residual adenoma after TURP may cause more prominent symptoms leading to higher retreatment rates. The incidence of ED after TURP for BPH is

still debated. It has been reported to occur in 4-35% of the patients.^{23,24} A higher incidence of postoperative ED was observed in the diabetics in our study. Our data were supported by other studies that have indicated a higher incidence of postoperative ED in diabetics.²⁵

To the best of our knowledge, there is no published study to interpret the results of the prostatectomy in diabetics. In this study, the limited number of the diabetics along with ignoring the objective parameters such as the peak flow rate and the pressure flow study could be considered as the major shortcomings of the study, however, the prospective design of the study and the longtime follow-up period, are certainly its major strengths. Also safety and efficacy of prostatectomy in diabetic patients and higher rate of reoperation in long term follow up were notable consequences in our study which has less been evaluated in previous studies.

We strongly recommend a similar study to be carried out with more cases using objective tools.

Conclusions

Our data indicate that surgery is beneficial for diabetics with severe lower urinary tract symptoms. Although a statistically significant greater reduction of IPSS was detected in nondiabetics when compared with diabetics 6 months after surgery, however, the improvement in both groups was significant. TURP is a safe procedure in such patients, and is not associated with a higher incidence of perioperative or postoperative complications, except for the postoperative ED and retreatment rates that seems to be higher in diabetics.

References

1. Glynn RJ, Campion EW, Bouchard GR, Silbert JE. The development of benign prostatic hyperplasia among volunteers in the Normative Aging Study. *Am J Epidemiol* 1985; 121: 78-90.
2. Arrighi HM, Metter EJ, Guess HA, Fozzard JL. Natural history of benign prostatic hyperplasia and risk of prostatectomy. The Baltimore Longitudinal Study of Aging. *Urology* 1991; 38 (1 Suppl): 4-8.
3. Cowie CC, Rust KF, Byrd-Holt DD, Eberhardt MS, Flegal KM, Engelgau MM, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health And Nutrition Examination Survey 1999-2002. *Diabetes Care*. 2006; 29: 1263-8.
4. Michel MC, Mehlburger L, Schumacher H, Bressel HU, Goepel M. Effect of diabetes on lower urinary tract symptoms in patients with benign prostatic hyperplasia. *J Urology* 2000; 163: 1725-9.
5. Hammarsten J, Hogstedt B. Hyperinsulinaemia as a risk factor for developing

- benign prostatic hyperplasia. *Eur Urol* 2001; 39: 151-8.
6. Burke JP, Jacobson DJ, McGree ME, Roberts RO, Girman CJ, Lieber MM, et al. Diabetes and benign prostatic hyperplasia progression in Olmsted County, Minnesota. *Urology* 2006; 67: 22-5.
7. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery -- executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation* 2002; 105: 1257-67.
8. Luttwak Z, Lask D, Abarbanel J, Manes A, Paz A, Mukamel E. Transvesical prostatectomy in elderly patients. *J Urology* 1997; 157: 2210-1.
9. Vagner EA, Goriunov VG, Davidov MI. [The results of prostatic adenomectomy in patients with severe concomitant diseases]. *Khirurgia* 1998; 8: 40-4.
10. Turner WH, Brading AF. Smooth muscle of the bladder in the normal and the diseased state: pathophysiology, diagnosis and treatment. *Pharmacol Therapeutics* 1997; 75: 77-110.
11. Ozturk Y, Altan VM, Yildizoglu-Ari N. Effects of experimental diabetes and insulin on smooth muscle functions. *Pharmacol Rev* 1996; 48: 69-112.
12. Azadzi KM, Tarcan T, Siroky MB, Krane RJ. Atherosclerosis-induced chronic ischemia causes bladder fibrosis and non-compliance in the rabbit. *J Urology* 1999; 161: 1626-35.
13. Berger AP, Kofler K, Bektic J, Rogatsch H, Steiner H, Bartsch G, et al. Increased growth factor production in a human prostatic stromal cell culture model caused by hypoxia. *Prostate* 2003; 57: 57-65.
14. Ghafar MA, Puchner PJ, Anastasiadis AG, Cabelin MA, Buttyan R. Does the prostatic vascular system contribute to the development of benign prostatic hyperplasia? *Current Urol Reports* 2002; 3: 292-6.
15. Berger AP, Deibl M, Halpern EJ, Lechleitner M, Bektic J, Horninger W, et al. Vascular damage induced by type 2 diabetes mellitus as a risk factor for benign prostatic hyperplasia. *Diabetologia* 2005; 48: 784-9.
16. Berger AP, Bartsch G, Deibl M, Alber H, Pachinger O, Fritsche G, et al. Atherosclerosis as a risk factor for benign prostatic hyperplasia. *BJU Int* 2006; 98: 1038-42.
17. Felsen D, Dardashti K, Ostad M, Lemer ML, Gross SS, Chen J, et al. Inducible nitric oxide synthase promotes pathophysiological consequences of experimental bladder outlet obstruction. *J Urology* 2003; 169: 1569-72.
18. Kiptoon DK, Magoha GA, Owillah FA. Early postoperative outcomes of patients undergoing prostatectomy for benign prostatic hyperplasia at Kenyatta National Hospital, Nairobi. *East African Med J* 2007; 84 (9 Suppl): S40-4.
19. Ibrahim AI, el-Malik E, Ghali AM, Murad N, Saad M. Effect of age, comorbidity and type of surgery on perioperative complications and mortality of prostatectomy. *Br J Urol* 1995; 76: 341-5.
20. Taylor Z, Krakauer H. Mortality and reoperation following prostatectomy: outcomes in a Medicare population. *Urology* 1991; 38 (1 Suppl): 27-31.
21. Roos NP, Wennberg JE, Malenka DJ, Fisher ES, McPherson K, Andersen TF, et al. Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *N Engl J Med* 1989; 320: 1120-4.
22. Roos NP, Ramsey EW. A population-based study of prostatectomy: outcomes associated with differing surgical approaches. *J Urology* 1987; 137: 1184-8.
23. Soderdahl DW, Knight RW, Hansberry KL. Erectile dysfunction following transurethral resection of the prostate. *J Urology* 1996; 156: 1354-6.
24. Lindner A, Golomb J, Korzack D, Keller T, Siegel Y. Effects of prostatectomy on sexual function. *Urology* 1991; 38: 26-8.
25. Taher A. Erectile dysfunction after transurethral resection of the prostate: incidence and risk factors. *World J Urol* 2004; 22: 457-60.