

Incidence and Risk Factors of Post-Operative Depression in Patients Undergoing Transurethral Resection of Prostate for Benign Prostatic Hyperplasia

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Background: Benign prostatic hyperplasia (BPH) is a frequent-occurring disease in middle-aged and elderly men. This work is a prospective study and aims at exploring the incidence of post-operative depression and the potential risk factors of depression in a cohort of patients with BPH in China.

Methods: In this survey, 611 men who underwent transurethral resection of the prostate (TURP) were strictly selected at our institution from January 2016 to August 2019. Zung Self-rating Depression Scale was used for evaluation of depressive symptoms. Sociodemographic, clinical and other data were also collected.

Results: We found that 152/611 (24.9%) patients suffered from different degree of depression at 6 months after TURP, including mild symptoms (20.9%) and moderate/severe symptoms (3.9%). A total of 421 (68.9%) patients developed post-TURP erectile dysfunction (ED). The occurrence of depression was closely associated with marital status, education level, cigarette smoking, alcohol consumption, severity of lower urinary tract symptoms (LUTS), duration of BPH, erectile function, and comorbidities (such as diabetes, dyslipidaemia and bladder stone). The risk factors related to the severity of depression included widowed or single marital status, frequent alcohol consumption, moderate or severe LUTS, longer duration (> 5 years) of BPH, ED, urinary continence, and comorbidities such as diabetes and bladder stone.

Conclusion: Many risk factors are related to the occurrence of depression in patients undergoing TURP. Widowed or single marital status, frequent alcohol consumption, moderate or severe LUTS, longer duration of BPH, ED, urinary incontinence and comorbidities such as diabetes and bladder stone are connected with the increase odds of moderate or severe depressive symptom.

Keywords: benign prostate hyperplasia, BPH, transurethral resection of the prostate, TURP, depression, prevalence rate, risk factors

Introduction

The current Chinese population is aging rapidly, and society is paying more attention to the health of the elderly. Benign prostatic hyperplasia (BPH) is a frequent-occurring disease that eventually causes lower urinary tract symptoms (LUTS) in middle-aged and elderly men.¹ A total of 50% of men over 50 and 90% of men over 80 suffer from LUTS/BPH, but these patients usually lose consciousness or do not seek treatment.^{2,3} Transurethral resection of the prostate (TURP) is a minimally invasive alternative to open prostatectomy for BPH patients. For BPH

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patients with moderate or severe LUTS who need active treatment or fail or do not want to receive medication, TURP has always been an effective and safe method for the treatment of BPH.^{4–6}

However, merely improving urinary function does not indicate that treatment is beneficial, as more than 20% of patients experience adverse reactions after TURP.^{7,8} TURP can cause psychological burden like stress, depression, and anxiety, as well as sexual problems such as erection and ejaculation disorders. It is well known that depression adversely affects the life span and overall quality of patients. TURP is an effective treatment for BPH, which can minimize BPH-induced anxiety, depression and psychiatric illness.⁹ Nonetheless, the risk factors related to depression after TURP still exist and obscure, and the adverse psychological effects associated with TURP are still unclear. At the same time, there is a lack of understanding about the depression in patients undergoing TURP. It is worth noting that depression is related to a remarkable rise in the number of deaths. Thus, early detection, intervention, and treatment of post-operative depression are vital for high-risk patients.

This work was a prospective study aimed at exploring the incidence of post-operative depression in Chinese BPH patients and identifying its potential risk factors.

Patients and Methods

Patient Cohort

A total of 692 patients with LUTS were recruited in the First Affiliated Hospital of Anhui Medical University from January 2016 to August 2019. These LUTS patients all received TURP and were histologically identified as BPH. All participants were informed and gave written consent. The trials were conducted out according to the Declaration of Helsinki, and authorized by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University.

The urologist discussed the therapeutic schedule with the patients based on the latest examination results and the medical history of patients. In general, surgery was recommended for patients at normal risk. Whether the patient accepts TURP was the result of a joint consultation between the patient and his clinician, while considering the benefits and risks of the therapeutic schedule. All surgical operations were performed by experienced urologists under general anesthesia. The final diagnosis of BPH was dependent on the pathological results after TURP.

Patients were interviewed using a questionnaire covering baseline demographics prior to undergo TURP. All patients were followed up by the same clinician 6 months after the operation. The standardized and structured questionnaire was listed as follows.

Demographic Characteristics

Information on age, education (Nine-year compulsory education system), income (judged by the subjective self-evaluation of patients), occupation, marital status and lifestyle were investigated.

LUTS

The International Prostatic Symptoms Score (IPSS) in the Chinese version was used to evaluate the severity degree of LUTS of patients.¹⁰ The IPSS is the total of seven scores, ranging from 0 to 35. LUTS is divided into three groups according to standard cut-points: severe (score ≥ 20), moderate (score 8 to 19) and mild (score ≤ 7).

Self-Rating Depression Scale

The Self-rating Depression Scale (SDS) tool was used to evaluate the depressive symptom of patients.¹¹ According to the Chinese standards,¹² a score higher than 53 was considered as depression. Furthermore, the severity of depression was divided into mild (score 53–62), moderate (score 63–72) and severe (score ≥ 72).

International Index of Erectile Function

The International Index of Erectile Function (IIEF-5) questionnaire provided in Chinese containing five questions.¹³ Score below 22 points were diagnosed as erectile dysfunction (ED).¹⁴

For this analysis, exclusion criteria as follows: a history of sexual dysfunction; a former surgery of the bladder, prostate or urethra; urethral stricture; prostate or bladder cancer; chronic urinary tract infection; neurological diseases and psychiatric disorders.¹⁵

Statistical Analysis

The data were analyzed using SPSS 21.0 statistical software (IBM, Armonk, NY, USA). Number (constituent ratio) was selected to describe the categorical variables. Chi-square test was used to compare the significant difference between two groups. The Pearson's correlation was applied to analyze the correlation coefficient. Logistic regression model was utilized to analyze the correlation

between the influencing factors and depression. Difference was considered statistically significant at $P < 0.05$.

Results

Baseline Data Analysis

A total of 692 respondents were enrolled in this study, and we analyzed the data of these patients. According to the preset criteria for inclusion and exclusion, 43 patients were excluded in the first round. According to the postoperative pathological results, 11 cases of prostate cancer and 3 cases of bladder cancer were excluded. There were no death during the operation. During the follow-up period, 6 patients died of causes unrelated to the previous surgery, and 18 patients were lost to follow-up or unable to participate. Finally, 611 samples were remained for analyses (Figure 1). In all samples, most patients were 61–80 years old, accounting for about 78.4% (479) of the total patients. There were 351 (57.4%) respondents who were married or in relationship. A total of 333 (54.5%) patients were current smokers and 208 (34.0%) patients were former smokers. In the meantime, a small number of subjects 133 (21.8%) drank alcohol regularly (Table 1).

In addition, 410 (67.1%) respondents had a history of BPH for more than 3 years. After the TURP therapy, 409 (66.9%) patients exhibited mild LUTS, 137 (27.3%) patients had moderate LUTS and 65 (10.7%) patients showed severe LUTS. This study also explored some common comorbidities, and the incidence of these comorbidities was shown as follows: 492 (80.5%) cases of hypertension, 233 (38.1%) cases of dyslipidaemia, 216 (35.4%) cases of coronary artery disease, 179 (29.3%) cases of type 2 diabetes, and 67 (11.0%) cases of bladder stone. At the same time, five patients suffered from persistent urinary incontinence (Table 2). The cause of urinary incontinence is probably urethral sphincter injury caused by surgery.

ED

The prevalence, demographic data and clinical factors of ED were shown in Tables 2 and 3. In the surveyed population, there were 421 (68.9%) patients developed post-operative ED, while few patients requested treatment. Our results revealed that the incidence of ED was in connection with the increasing age, widowed or single marital status, reduced physical activity (such as sedentary lifestyle), current smoking, frequent drinking, severity of LUTS, comorbidities (such as obesity, diabetes, coronary artery disease, and dyslipidaemia), and the occurrence of depression.

Depression Symptoms

According to the SDS, we found that 152 (24.9%) patients with BPH suffered from different degrees of depression 6 months after TURP, including 20.9% of mild Depression symptoms (DSs) and 3.9% of moderate/severe DSs. Moreover, the occurrence of depression was closely associated with marital status, education, smoking, drinking, LUTS, duration of BPH, ED, urinary incontinence and comorbidities (such as diabetes, dyslipidaemia and bladder stone).

According to the logistic regression analysis, we evaluated the risk factors related to depression severity as follows: widowed or single marital status (odds ratio [OR] = 4.73; 95% confidence interval [CI] = 1.67–13.46, $P = 0.004$), frequent alcohol consumption (OR = 5.44; 95% CI = 2.17–13.68; $P < 0.001$), moderate or severe LUTS (OR = 3.12; 95% CI = 1.21–8.05; $P = 0.018$), longer duration (> 5 years) of BPH (OR = 3.51; 95% CI = 1.31–9.42; $P = 0.013$), erectile dysfunction (OR = 8.32; 95% CI = 1.08–63.99; $P = 0.042$), urinary continence (OR = 5.88; 95% CI = 3.23–10.70; $P = 0.002$), and comorbidities such as diabetes (OR = 2.87; 95% CI = 1.18–6.99; $P = 0.021$), bladder stone (OR = 4.52; 95% CI = 1.69–12.12; $P = 0.003$). Moreover, logistic regression analysis also showed that mild and moderate/severe depression patients had no significant differences in the education, cigarette smoking, and dyslipidaemia.

Discussion

BPH is a common and highly prevalent disease, but it is not life-threatening.¹⁶ However, it has been frequently reported that patients with BPH suffered from LUTS, stress, anxiety, depression, and incapacity to complete basic tasks due to the psychological impacts.^{17–20} Previous studies on BPH patients who undergoing TURP only emphasized the examination of postoperative comorbidities or the technical success of the operation, whereas seldom paid attention to the correlations between TURP treatments for BPH and the adverse psychological effects.

Depression is another common and familiar disease that seriously affects the quality of life. According to data from the National Institute of Mental Health, the prevalence of depression is about 16.5%.²⁰ Due to the serious negative impact of depression on the physical and mental health of patients, it has always been a public health problem that deserves worldwide attention.²¹ In the present study, we systematically evaluated the incidence of

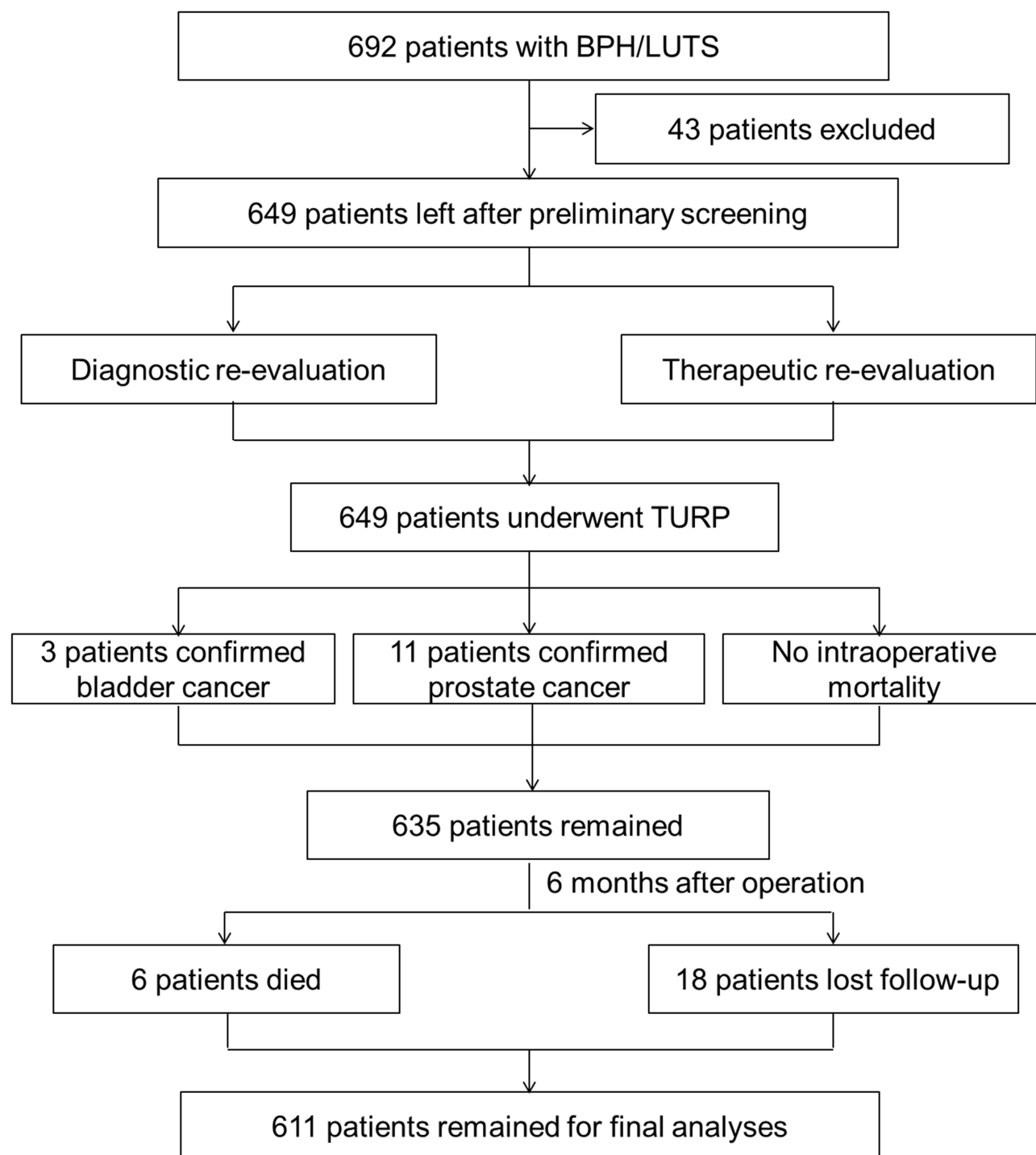


Figure I Flow chart of participant enrolment.

post-operative depression in Chinese men and identified the potential risk factors.

Many studies have demonstrated that BPH/LUTS can increase the likelihood of depression. Coyne et al²² have found that moderate/severe LUTS is significantly associated with an increased risk of depression. Furthermore,

another population-based cross-sectional study also has revealed that depression is a common disease in men with LUTS.²³ Consistent with the previous findings, we also found that patients with LUTS were more likely to suffer from depression than patients without LUTS. In addition, results of multiple logistic regression analysis

Table I Frequency of Depression and Erectile Dysfunction in Relation to Baseline Characteristics of 611 Patients

	Total N=611	Without Depression		With Depression		P*	Erectile Dysfunction		P*
		N=459	%	N=152	%		N=421	%	
Age (years)						0.463			0.000 [‡]
≤ 60	72	54	75.0	18	25.0		38	52.8	
61–80	479	356	74.3	123	25.7		323	67.4	
> 80	60	49	81.7	11	18.3		60	100	
^a Duration of BPH (years)						0.016 [‡]			0.448
< 1	97	76	78.4	21	21.6		64	66.0	
1–3	104	85	81.7	19	18.3		66	63.5	
3–5	167	132	79.0	35	21.0		119	71.3	
> 5	243	166	68.3	77	31.7		172	70.8	
Marital status						0.032 [‡]			0.001 [‡]
Married	351	275	78.3	76	21.7		223	63.0	
Widowed/single	260	184	70.8	76	29.2		198	76.2	
Education						0.000 [‡]			0.158
> 9 years	325	264	81.2	61	18.8		232	71.4	
≤ 9 years	286	195	68.2	91	31.8		189	66.1	
Occupation						0.986			0.942
Retired/unemployed	575	432	75.1	143	24.9		396	68.9	
Employed	36	27	75.0	9	25.0		25	69.4	
^b Income						0.260			0.074
Insufficient	218	158	72.5	60	27.5		160	73.4	
Sufficient	393	301	76.6	92	23.4		261	66.4	
^c Nutritional status						0.198			0.000 [‡]
BMI < 24	404	310	76.7	94	23.3		238	58.9	
BMI ≥ 24	207	149	72.0	58	28.0		183	88.4	
Physical activity						0.478			0.000 [‡]
< 30 min/day	420	312	74.3	108	25.7		312	74.3	
≥ 30 min/day	191	147	77.0	44	23.0		109	57.1	
^d Cigarette smoking						0.001 [‡]			0.000 [‡]
Currently	333	230	69.1	103	30.9		259	77.8	
Ever	208	172	82.7	36	17.3		119	57.2	
Never	70	57	81.4	13	18.6		43	61.4	
Alcohol consumption						0.025 [‡]			0.017 [‡]
Frequently (≥ 3 per week)	133	88	66.2	45	33.8		104	78.2	
Seldom	348	269	77.3	79	22.7		236	67.8	
Never	130	102	78.5	28	21.5		81	62.3	

Notes: ^aDuration of BPH was defined as the time from LUTS onset to the operation date. ^bInsufficient income was defined as patients reported difficulty to make both ends meet; ^cAccording to Chinese standards, BMI ≥ 24 was defined as overweight; ^dFailure to quit smoking was defined as currently, former smokers was defined as ever; Never smoking was defined as never. *Difference between two subgroups was assessed by Chi-square test. [‡]The difference was statistically significant.

Abbreviations: BPH, benign prostatic hyperplasia; BMI, body mass index (kg/m²); LUTS, lower urinary tract symptoms.

indicated that there was significant association between the severity of LUTS and moderate/severe depression after TURP treatment. Obviously, LUTS is a risk factor predicting the occurrence of depression, which means that the negative effects of LUTS may be responsible for the

occurrence, development and progression of depression.²⁴ Previous study has reported that post-prostatectomy urinary incontinence may be temporary damage and can be resolved spontaneously.²⁵ Most patients will recover from urinary incontinence within 6 months after surgery. Here,

Table 2 Severity of LUTS, Coexisting Diseases, Erectile Function and Depression in Patients with BPH at 6 Months After TURP

	Total N=611	Without Depression		With Depression		P*	Erectile Dysfunction		P*
		N=459	%	N=152	%		N=421	%	
Severity of LUTS currently						0.000 [‡]			0.000 [‡]
Mild	409	330	80.7	79	19.3		239	58.4	
Moderate	137	89	65.0	48	35.0		121	88.3	
Severe	65	40	61.5	25	38.5		61	93.8	
Comorbidities									
Coronary artery disease	216	156	72.2	60	27.8	0.220	165	76.4	0.003 [‡]
Diabetes	179	123	68.7	56	31.3	0.018 [‡]	151	84.4	0.000 [‡]
Hypertension	492	364	74.0	128	26.0	0.185	340	69.1	0.826
Dyslipidaemia	233	164	70.4	69	29.6	0.033 [‡]	182	78.1	0.000 [‡]
Bladder stone	67	43	64.2	24	35.8	0.028 [‡]	45	67.2	0.744
Erectile function [pts.]						0.013 [‡]			NA
IIEF-5 <22	421	304	72.2	117	27.8		–	–	
IIEF-5 ≥22	190	155	81.6	35	18.4		–	–	
Urinary incontinence						0.001 [‡]			0.331
Yes	5	0	0	5	100		5	100	
No	606	459	75.7	147	24.3		416	68.6	
Depression symptoms						NA			0.000 [‡]
No symptoms	459	459	100	–	–		304	66.2	
Mild	128	–	–	128	84.2		94	73.4	
Moderate	20	–	–	20	13.2		19	95.0	
Severe	4	–	–	4	2.6		4	100	

Notes: *Difference between two subgroups was assessed by Chi-square test. [‡]The difference was statistically significant.

Abbreviations: LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia; TURP, transurethral resection of the prostate; IIEF-5, International Index of Erectile Function questionnaire-5.

our results confirmed that 5 patients developed persistent incontinence 6 months after surgery. The cause of urinary incontinence was probably urethral sphincter injury caused by surgery. Importantly, urinary incontinence increased the risk of moderate/severe depression. In addition, LUTS can indirectly cause depression through sleep deprivation, because nocturia is one of the major symptoms of LUTS.²⁶

At least 85.5% of depression patients suffer from ED, which is the most common sexual dysfunction after TURP. However, about 83% of men over the age of 50 maintain sexual activity, and thus these patients are more prone to depression and dissatisfaction with post-operative erectile function.²⁷ ED seriously affects the self-esteem of patients, which may lead to the development of depression.²⁸ Consistent with the former studies,^{29–31} we demonstrated that ED was closely associated with advancing age, widowed or single, obesity (BMI ≥ 24), sedentary lifestyle (physical inactivity), current cigarette smoking, frequent alcohol consumption, moderate or severe LUTS, and comorbidities such as coronary artery disease, diabetes

and dyslipidaemia. Patients with moderate/severe LUTS had a significant increased risk of ED and the risk of depression had almost doubled.

At present, both smoking and frequent alcohol consumption are main risk factors that increase the prevalence of depression.^{32,33} Meanwhile, lack of physical activity and obesity are related to depression.^{34,35} However, in our study, it was observed that lack of physical activity and obesity had no influence on depression. It should be emphasized that widowed or single men had the higher degree of depression. Many researches have confirmed that widowhood and single men around the world are more likely to suffer from depression.^{36,37} Whether long-term lack of a sexual partner is the cause of depression is unclear, and further researches are needed.

Urology clinicians should understand that LUTS/BPH and depression are usually comorbid.³⁸ Our results indicated that the prevalence of post-operative depression among in BPH patients was approximately 24.9%. It is very necessary to screen all patients for depression after

Table 3 Risk Factors Revealed by Multiple Logistic Regression for Severity of Depression Symptoms

Risk Factors	Subgroup	Depression Symptoms		OR (95% CI)	Significance*
		Mild N (%)	Moderate or Severe N (%)		
Marital status	Married Widowed/single	71 (93.4) 57 (75.0)	5 (6.6) 19 (25.0)	1.00 4.73 (1.67–13.46)	0.004 [‡]
Education	> 9 years ≤ 9 years	81 (89.0) 47 (77.0)	10 (11.0) 14 (23.0)	1.00 0.41 (0.17–1.01)	0.052
Cigarette smoking	Ever/Never Currently	44 (89.8) 84 (81.6)	5 (10.2) 19 (18.4)	1.00 1.99 (0.70–5.69)	0.199
Alcohol consumption	Seldom/Never Frequently	98 (91.6) 30 (66.7)	9 (8.4) 15 (33.3)	1.00 5.44 (2.17–13.68)	0.000 [‡]
Severity of LUTS	Mild Moderate/Severe	72 (91.1) 56 (76.7)	7 (8.9) 17 (23.3)	1.00 3.12 (1.21–8.05)	0.018 [‡]
Duration of BPH	≤ 5 years > 5 years	69 (92.0) 59 (76.6)	6 (8.0) 18 (23.4)	1.00 3.51 (1.31–9.42)	0.013 [‡]
Erectile function	IIEF-5 ≥ 22 IIEF-5 < 22	34 (97.1) 94 (80.3)	1 (2.9) 23 (19.7)	1.00 8.32 (1.08–63.99)	0.042 [‡]
Urinary incontinence	No Yes	127 1	20 4	1.00 5.88 (3.23–10.70)	0.002 [‡]
Diabetes	No Yes	86 (89.6) 42 (75.0)	10 (10.4) 14 (25.0)	1.00 2.87 (1.18–6.99)	0.021 [‡]
Dyslipidaemia	No Yes	71 (85.5) 57 (82.6)	12 (14.5) 12 (17.4)	1.00 1.25 (0.52–2.98)	0.622
Bladder stone	No Yes	113 (88.3) 15 (62.5)	15 (11.7) 9 (37.5)	1.00 4.52 (1.69–12.12)	0.003 [‡]

Notes: *Difference between two subgroups was assessed by logistic regression analysis. [‡]Statistical significant after logistic regression analyses.

Abbreviations: LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia; IIEF-5, International Index of Erectile Function questionnaire-5; OR, odds ratio; CI, confidence interval.

TURP. The results suggested that interventions may assist patients planning to undergo TURP, especially those who screened for positive risk factors for depression. The post-TURP response for LUTS/BPH may also be improved by combating the potential depression.

Unlike other diseases, the lesions in urology patients are located in the genitourinary tract. During the endoscopic standard procedures, the patient who undergoes regional anesthesia is awake, and the reproductive organs will be exposed, so that the patient is more likely to show anxiety and stress and other emotions.³⁹ Complementary therapies to decrease the pain and anxiety during endoscopic standard procedures are becoming more popular day by day. These therapies include music, transcutaneous electrical nerve stimulation, acupuncture, and auricular acupressure.

The least invasive of these therapies is music. In recent years, music therapy has been widely used in various mental disorders and has a good auxiliary treatment effect on anxiety. Music therapy can improve anxiety and depression, and enhance initiative of patients.^{40,41} The effect of music as a potential tool for improving the quality of life on anxiety or depression in cancer patients and/or on pain perception in standard procedures for BPH such as endorectal ultrasound or cystoscopy are already recognized several decades ago.^{42,43} Therefore, music may be used as a complementary therapy to relieve anxiety in patients during the endoscopic standard procedures.

In our study, we integrated multiple factors related to post-operative depression in patients who undergoing TURP. However, we have to acknowledge that there are

some limitations in this research. For instance, a minority of patients was involved in our study. Our results may not extend to the whole Chinese male population. Furthermore, there was no patient in control group (other treatment options). Nevertheless, the study was conducted by the research institute in the local community, thereby facilitating consistent follow-up actions. Further studies may clarify the relationship and causality between TURP and post-operative depression.

Conclusion

In summary, many risk factors related to disease courses, lifestyle, even comorbidities are related to the occurrence of depression in patients who undergoing TURP. Especially widowed or single marital status, frequent alcohol consumption, moderate or severe LUTS, longer duration of BPH, ED, urinary incontinence and comorbidities such as diabetes and bladder stone are associated with increased odds of moderate/severe depression.

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Disclosure

The authors declared no conflicts of interest.

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