



# Holter Monitoring (24-Hour ECG) Parameter Dynamics in Patients with Ischemic Heart Disease and Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia

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## ABSTRACT

**Introduction:** This study examined the dynamics of 24-h electrocardiogram (ECG) monitoring parameters (Holter monitoring) in patients with ischemic heart disease (IHD) before and after conservative or surgical treatment of patients with voiding and storage lower urinary tract symptoms (LTS) due to benign prostatic hyperplasia (BPH).

**Methods:** A total of eighty-three 57 to 81-year-old (mean age  $70.4 \pm 5.75$  years) patients with LTS/BPH and accompanying IHD were examined and treated at the Institute of Urology and Human Reproductive Health and Clinic of Cardiology of Sechenov University. All patients

received recommended cardiac therapy at least 6 months before inclusion in the study.

**Results:** Our study demonstrated that there is correlation between voiding and storage LUTS/BPH and Holter-detected cardiac impairments in patients with IHD/BPH. These data make it possible to consider LUTS/BPH (voiding and storage) as a factor in the additional functional and psychological load on the activity of patients with ischemic heart disease. Improvement of voiding and storage LUTS due to BPH and objective parameters of urination ( $Q_{max}$ ) in patients treated with alpha-1 adrenoceptor blocker tamsulosin correlated with improvement of 24-h ECG monitoring parameters (Holter monitoring) in 72% of patients. Improvement of 24-h ECG monitoring parameters (Holter monitoring) 1 month after transurethral resection of the prostate (TURP) in IHD/BPH patients and indications for surgical treatment was observed in 65.7%. Negative dynamics of the Holter-based ECG was not registered in patients who were operated on.

**Conclusion:** Holter monitoring helps to identify groups of patients in whom urinary impairments caused by prostatic hyperplasia negatively affect the course of IHD. Restored urination (either conservatively or operatively) in patients with BPH in 72% of cases decreased the number of fits of angina, thus influencing favourably the course of IHD.

**Trial Registration:** ClinicalTrials.gov Identifier: NCT03856242.

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**Keywords:** Alpha-1-adrenoblockers; Benign prostatic hyperplasia (BPH); Cardiac rhythm; Holter monitoring (HM); Ischemic heart disease (IHD); Lower urinary tract symptoms (LUTS); Transurethral resection of the prostate (TURP); Voiding dysfunctions

## INTRODUCTION

The frequency and severity of the ischemic heart disease (IHD) and lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) increase with aging [1].

The correlation between frequency and severity of IHD and frequency and severity of LUTS/BPH has been presented already. Karatas et al. reported that patients with LUTS/BPH have a considerably higher prevalence of cardiovascular disease than the general population in old age without LUTS. LUTS/BPH causing nocturia-induced sleep disturbances, arterial blood pressure variability, and increased sympathetic activity may be an insidious risk factor for IHD. An understanding of the impact of LUTS/BPH may produce a new approach to treatment [2].

Wehrberger et al. examined 2092 patients and determined that the 10-year risk for IHD in men with severe, moderate and mild LUTS was 15.9%, 10.6% and 8.8%, respectively ( $p < 0.01$ ) [3].

Gacci et al. demonstrated that the presence of moderate to severe LUTS significantly increased the risk of cardiovascular events in male subjects ( $p < 0.001$ ) [4].

Patients with LUTS/BPH and IHD may experience cardiac pain during obstructed urination [5–7].

## METHODS

A total of eighty-three 57- to 81-year-old (mean age  $70.4 \pm 5.75$  years) patients diagnosed with IHD and accompanying LUTS/BPH were examined at the Institute of Urology and Human Reproductive Health and Clinic of Cardiology of Sechenov University.

All patients had LUTS with the International Prostate Symptom Score (IPSS) of 8 or more. The severity of BPH symptoms and patients' quality of life were assessed by means of the IPSS and QoL questionnaires. Uroflowmetry was used to determine the degree of impairments of urination. Prostate volume and amount of residual urine were measured during transabdominal ultrasound examination (if necessary also transrectal ultrasound), as well as digital rectal examination and blood analysis for prostate-specific antigen (PSA) and, if indicated, biopsy of the prostate to rule out cancerous prostatic lesion. In all patients the prostate was enlarged ( $> 30$  cc) according to ultrasound measurements and obstructive urination was determined according to uroflowmetry ( $Q_{\max} < 12$  ml/s).

Beside undergoing interviews (in the presence of angina, the patients filled in the Seattle Angina Questionnaire, SAQ), the patients were subjected to measurement of arterial pressure on both arms, biochemical blood analysis (measuring the level of triglycerides, cholesterol, if necessary, high-, low- and very-low-density lipoproteins) and standard 12-lead electrocardiogram (ECG). In order to verify the diagnosis of IHD, all patients underwent detailed examination in the setting of a cardiology hospital. The following studies, if indicated, were performed: treadmill, stress echocardiography, coronarography and spiral computed tomography of the coronary arteries. All patients received recommended cardiac therapy at least 6 months before inclusion in the study.

The key method in our study was 24-h ECG (Holter) monitoring using the Schiller MT 200 device (Switzerland). Deciphering the data of 24-h ECG monitoring, we examined the dynamics of the ST segment and changes in the cardiac rhythm during urination, which was registered by the patient by pressing the button on the device and keeping a diary, and overall during the whole period (24 h) of Holter monitoring.

All patients were included in the study according to following inclusion criteria.

## Inclusion Criteria

(1) Patient's consent; (2) absence of severe comorbidity hampering the ability to carry out the study (mental disorders, musculoskeletal system diseases, oncological diseases); (3) LUTS/BPH, with a total score by IPSS of 8 or more; (4)  $Q_{\max}$  according to uroflowmetry less than 12 ml/s; (5) prostate enlargement (> 30 cc) according to ultrasound measurements; (6) functional class II–IV angina of effort; (7) non-ST segment depression postinfarction cardiosclerosis, (8) receiving recommended cardiac therapy at least 6 months before inclusion in the study.

## Exclusion Criteria

(1) Presence of suprapubic drainage; (2) long-term pharmacological therapy of LUTS/BPH (alpha adrenoceptor blockers, 5-alpha-reductase inhibitors and others)—for the groups of patients receiving conservative treatment of BPH; (3) patients after surgical treatment of prostatic hyperplasia (TURP or simple prostatectomy); (4) urinary bladder stones; (5) acute urinary retention; (6) changes on the ECG hampering its interpretation (complete left bundle branch block, cicatricial changes after endured myocardial infarction, permanent form of ciliary arrhythmia); (7) acute forms of ischemic heart disease.

## Criterion for Withdrawal

Voluntary refusal of the patient to undergo further treatment or follow-up.

Depending on the results of primary Holter monitoring (HM) and the method of correction (pharmacological or surgical) of LUTS/BPH, all patients were divided into three groups:

Group 1 ( $n = 20$ ) Included patients in whom primary HM revealed ECG alterations appearing or deteriorating during urination. To improve impaired urination, all group 1 patients, along with recommended cardiotropic therapy, received tamsulosin 0.4 mg once daily (in the morning) for 1 month—the whole period of follow-up and treatment.

Group 2 ( $n = 28$ ) Patients who had HM-detected significant ECG alterations; however, the alterations were unrelated to the act of urination as compared with group 1. To improve impaired urination, these patients, along with the recommended cardiac therapy, received tamsulosin 0.4 mg once daily (in the morning) for the whole period of follow-up and treatment.

Group 3 ( $n = 35$ ) Consisted of patients with severely obstructed urination (I-PSS > 25) and IHD found to have pronounced impairments. Like in group 2, HM demonstrated significant changes in the ECG unrelated to the act of urination.

Surgical treatment comprised transurethral resection of the prostate (TURP).

After a month of conservative treatment we evaluated the subjective symptomatology by the IPSS and QoL scales, performed uroflowmetry, ultrasound examination of the prostate and the volume of residual urine, standard ECG and repeat 24-h ECG monitoring with registration of the time of urination. All patients filled in the SAQ again.

The subjective symptomatology of patients in group 3 was evaluated at 1 month after surgery and continuing cardiac therapy by the IPSS and QoL scales. The uroflowmetry, ultrasound examination of the prostate and the volume of residual urine, standard ECG and repeat 24-h ECG monitoring with registration of the time of urination were performed. All patients filled in the SAQ again. The data were processed using the methods of descriptive statistics, Student's *t* test for paired values, in the programme BIO-STAT [8].

All procedures performed in the study were in accordance with standard clinical care and were in accordance with the I. M. Sechenov First Moscow State Medical University IRB and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by I. M. Sechenov First Moscow State Medical University IRB Protocol Record 03-19 and was registered on ClinicalTrials.gov (NCT03856242). Informed consent was obtained from all individual participants included in the study.

## RESULTS

### Group 1 (n = 20)

The group 1 patients' age varied from 63 to 79 years (mean  $68.6 \pm 4.94$  years).

Cardiovascular diseases in group 1 patients are listed in Table 1. Eighteen (90%) patients from this group received recommended cardiac therapy which was started at least 6 months before inclusion in the study and did not change during 1-month follow-up.

For the treatment of LUTS/BPH all patients in group 1 received tamsulosin 0.4 mg once a day in the morning during 1 month. All of them showed improvement of subjective and objective symptoms of voiding dysfunctions. Mean values of the subjective and objective parameters of urination before and after therapy with tamsulosin 0.4 mg are given in Table 2 and Fig. 1.

Fourteen of the 20 patients (70%) from this group were found to have “angina of effort” and they filled in the SAQ before and after tamsulosin therapy. Table 3 and Fig. 2 show the parameters of the SAQ in patients with positive dynamics ( $n = 9$ ) and without dynamics ( $n = 5$ )

of the clinical course of “angina of effort” in patients with improved urination.

As can be seen from Table 3 and Fig. 2, the mean value of the SAQ total score in nine patients with “angina of effort” significantly improved from  $64.7\% \pm 5.1\%$  before treatment to  $72.5\% \pm 5.7\%$  ( $p < 0.02$ ) after 1 month of tamsulosin administration. The remaining five patients (Table 3) with “angina of effort” during the initial HM had ST segment depression, severe cardiac pathology and demonstrated no significant change of the SAQ score for angina ( $p = 0.1$ ). Three of them were operated on.

According to the follow-up HM in 15 patients the improvement of urination was associated with positive dynamics of Holter-derived ECG, manifesting as either disappearance of urination-related HM changes ( $n = 14$ ) or a decrease in the degree of these changes ( $n = 1$ ). Also, all 15 patients were found to have a decreased number of ST segment depressions and the number of supraventricular extrasystoles (SVE) and ventricular extrasystoles (VE) in absolute terms (Table 4).

In one patient with initial ST segment depression at the moment of urination of up to 3.1 mm, ST segment depressions were preserved

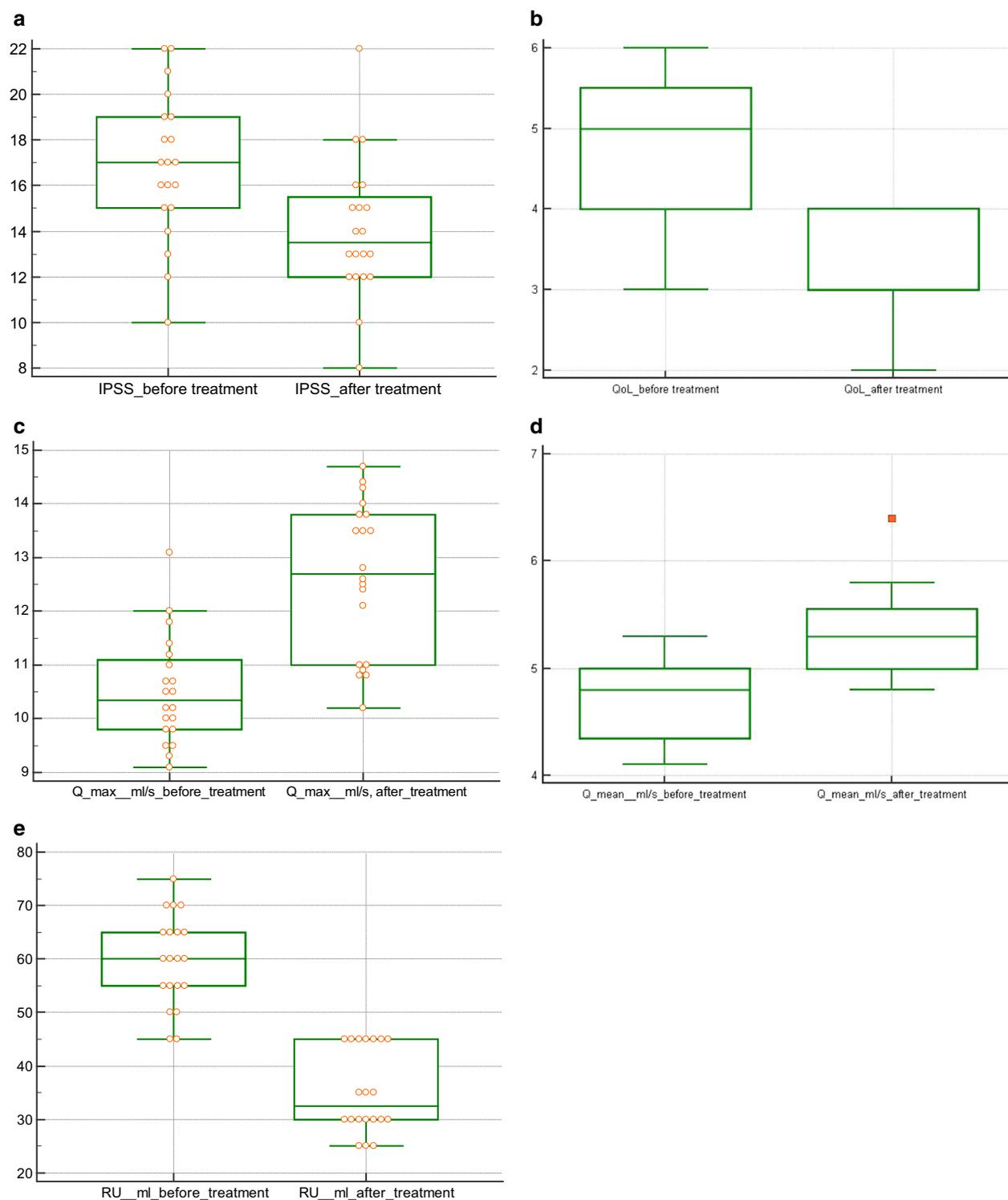
**Table 1** Cardiovascular diseases in group 1 patients

Cardiovascular diseases	Quantitative assessment (n = 20)	
	Number	Percentage
Postinfarction atherosclerosis	10	50
FC II angina of effort	6	30
FC III angina of effort	8	40
Ventricular extrasystole	5	25
Supraventricular extrasystole	8	40
Paroxysmal ciliary arrhythmia	5	25
First-degree atrioventricular block	3	15
Left anterior bundle branch block	2	10
Stage II arterial hypertension	6	30
Stage III arterial hypertension	7	35

**Table 2** Dynamics of subjective and objective parameters of urination before and on the background of therapy with tamsulosin in group 1 patients (n = 20)

Parameters of LUTS/BPH	Before treatment	After treatment	p
IPSS	17 (10–22)	13.5 (8–22)	0.001
QoL	5 (3–6)	3 (2–4)	0.003
$Q_{max}$	10.3 (9.1–13.1)	12.7 (10.2–14.7)	0.0001
$Q_{mean}$	4.8 (4.1–5.3)	5.3 (4.8–6.4)	0.0001
RU	60 (45–75)	32.5 (25–45)	0.068

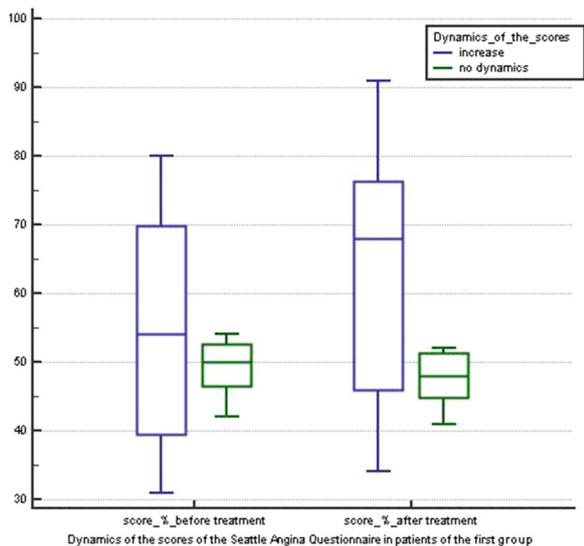
IPSS International Prostate Symptom Score, QoL quality of life related to LUTS,  $Q_{max}$  peak urinary flow rate measured by uroflowmetry (ml/s),  $Q_{mean}$  average urinary flow rate measured by uroflowmetry (ml/s), RU volume of residual urine in the urinary bladder on ultrasonography (measured in millilitres)



**Fig. 1** Mean value of subjective and objective parameters of urination before and after therapy with tamsulosin 0.4 mg in patients of the first group: **a** IPSS; **b** QoL; **c** Q max; **d** Q mean; **e** RU

**Table 3** Dynamics of the scores of the Seattle Angina Questionnaire in patients of group 1

	Min. score (%)	Max. score (%)	Mean value (%)
Before treatment (n = 9)	31	80	64.7 ± 5.1
After treatment (n = 9)	34	91	72.5 ± 5.7
Before treatment (n = 5)	42	54	49.0 ± 2.4
After treatment (n = 5)	41	52	48.4 ± 0.5



**Fig. 2** Dynamics of the scores of the Seattle Angina Questionnaire in patients of the first group

at 1 month after treatment with tamsulosin; however, they were not more than 1 mm.

In the remaining five patients, despite improved urination, ST segment depression both on the background thereof and generally was preserved. Two of these patients underwent coronarography revealing diagnostically significant stenosis of three coronary vessels. They were therefore advised to undergo operative treatment for IHD. Also, these two patients had stage 3 arterial hypertension, functional class

**Table 4** Predominant alterations in HM parameters and their dynamics before and after treatment of BPH in IHD patients of group 1

n = 20	Before treatment of LUTS/BPH	After treatment of LUTS/BPH
ST segment depression (1 mm)	4	0
ST segment depression (2 mm)	10	0
ST segment depression (3.1 mm)	1	1
SVE	4	0
VE	1	0

II–III angina pectoris. One of the five patients was found to have a history of postinfarction cardiosclerosis, functional class III “angina of effort”, and aortocoronary bypass grafting. The remaining two patients had functional class III angina, stage III arterial hypertension and one patient also had postinfarction cardiosclerosis and the other one had a history of aortocoronary bypass grafting.

**Group 2 (n = 28)**

This group enrolled 28 patients in whom primary HM detected certain alterations (VE, SVE, ST segment depression), which did not coincide with the act of urination. The age of patients was from 57 to 81 years (mean 71.3 ± 1.1 years). Cardiovascular diseases in patients of group 2 are listed in Table 5.

Urination improved in all patients of this group on the background of tamsulosin therapy. Table 6 and Fig. 3 reflect the mean values of subjective and objective parameters of urination before and after tamsulosin therapy.

Seventeen of the 28 patients of this group had “angina of effort”, hence they filled in the SAQ before and after tamsulosin therapy.

**Table 5** Cardiovascular diseases in the patients of group 2

Cardiovascular diseases	Quantitative assessment ( <i>n</i> = 28)	
	Number	Percentage
Postinfarction atherosclerosis	12	42.8
FC I angina of effort	0	0
FC II angina of effort	8	28.5
FC III angina of effort	9	32.1
Ventricular extrasystole	14	50
Supraventricular extrasystole	22	78.6
Paroxysmal ciliary arrhythmia	4	14.3
First-degree atrioventricular block	3	10.7
Left bundle branch block	2	7.1
Stage II arterial hypertension	13	46.4
Stage III arterial hypertension	6	21.4

Table 7 and Fig. 4 show the SAQ scores, which in 11 patients were characterized by a statistically significant increase (from  $61.3\% \pm 3.2\%$  to  $69.6\% \pm 3.4\%$ ;  $p < 0.01$ ) and in six patients remained unchanged ( $52.8\% \pm 2.8\%$  vs  $53.5\% \pm 3.6\%$ ;  $p > 0.06$ ).

According to the HM findings in this group of patients ( $n = 28$ ) various changes on the ECG (SVE, VE and ST segment depression) did not coincide with urination. As mentioned above, all patients of this group demonstrated subjectively and objectively improved parameters of urination after 1 month therapy with tamsulosin (Table 6 and Fig. 3). In 20 patients, it was also accompanied by positive dynamics of the Holter-derived ECG. This was characterized by either disappearance of ST segment depression ( $n = 5$ ) or a decrease in the absolute number of extrasystoles ( $n = 15$ ), or a decreased degree of these changes ( $n = 1$ ). Fifteen patients were found to have a decrease in the number of ST segment depressions and the absolute number of supraventricular and ventricular extrasystoles (Table 8).

In one patient with ST segment depression, the latter was also preserved after therapy with

**Table 6** Dynamics of subjective and objective parameters of urination before and after tamsulosin therapy in patients of group 2 ( $n = 28$ )

Parameters of LUTS/BPH	Before treatment	After treatment	<i>p</i>
IPSS	17 (12–23)	14 (10–18)	0.0001
QoL	5 (3–6)	3 (2–4)	0.0001
$Q_{\max}$	10.5 (9.5–13.2)	13.1 (10.8–14.6)	0.0001
$Q_{\text{mean}}$	4.8 (4.2–5.5)	5.2 (4.8–6.6)	0.0001
RU	60 (45–70)	35 (25–45)	0.001

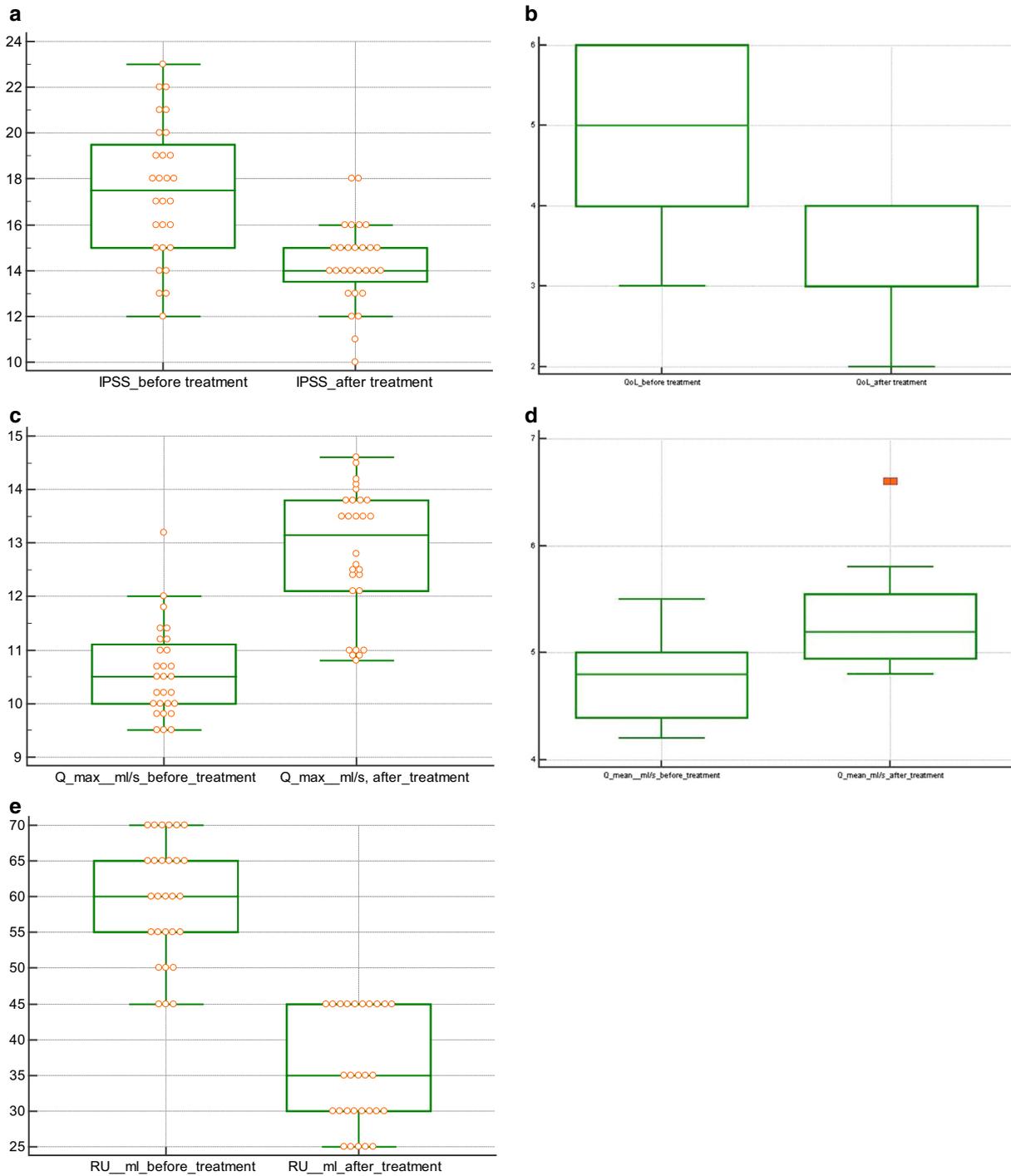
tamsulosin. This patient was diagnosed as having subtotal stenosis of the left coronary artery and multiple stenosis of two other coronary arteries. The patient continued taking tamsulosin until coronary artery bypass grafting was carried out.

In seven patients the Holter-based ECG remained without dynamics 1 month after therapy with tamsulosin (Table 8).

Patients demonstrating no positive dynamics of the Holter-derived ECG had both more pronounced cardiac pathology and a greater number of extrasystoles during 24 h of monitoring. Three of the seven patients, in whom heart rhythm abnormalities persisted even a month after tamsulosin therapy, required operative treatment of IHD. Two of them underwent surgery at 1 and 1.5 months after they started taking tamsulosin.

### Group 3 ( $n = 35$ )

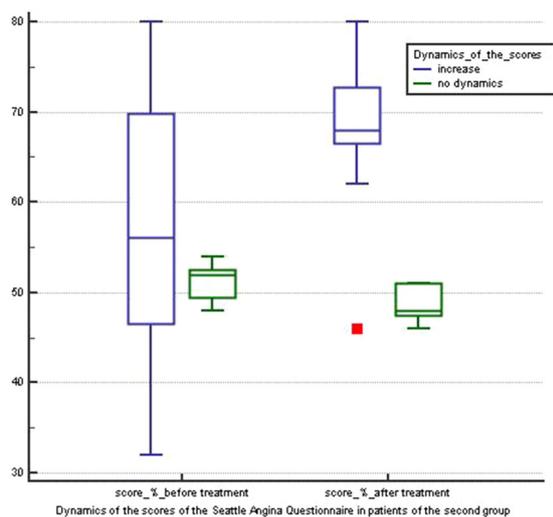
This group comprised patients for whom after examination for symptoms of IHD and LUTS/BPH a decision was made on the necessity to perform operative treatment of BPH. TURP operation was indicated because of pronounced urination disorders which were most important amongst the patient's complaints. The patients' age varied from 59 to 77 years (mean  $67.5 \pm 2.1$  years). Cardiovascular diseases in patients of group 3 are listed in Table 9



**Fig. 3** Mean value of subjective and objective parameters of urination before and after therapy with tamsulosin 0.4 mg in patients of the second group: **a** IPSS; **b** QoL; **c** Q max; **d** Q mean; **e** RU

**Table 7** Dynamics of the Seattle Angina Questionnaire scores in group 2 patients

	Min. score (%)	Max. score (%)	Mean (%)
Before treatment ( <i>n</i> = 11)	39	76	61.3 ± 3.2
After treatment ( <i>n</i> = 11)	61	77	69.6 ± 3.4
Before treatment ( <i>n</i> = 4)	44	62	52.8 ± 2.8
After treatment ( <i>n</i> = 4)	42	67	53.5 ± 3.6

**Fig. 4** Dynamics of the scores of the Seattle Angina Questionnaire in patients of the second group

All patients received cardiotropic therapy before primary HM, and which remained unchanged until the control examination 1 month thereafter.

In all patients of this group urination improved 1 month after the TURP. Table 10 and Fig. 5 reflect the mean values of the subjective and objective parameters of urination before and after TURP for prostatic hyperplasia.

Twenty-three patients of group 3 were diagnosed as having “angina of effort”. The average

**Table 8** Predominant impairments of HM parameters and their dynamics before and after treatment of LUTS/BPH in group 2 patients with IHD

<i>n</i> = 28	Before treatment of LUTS/BPH	After treatment of LUTS/BPH
ST segment depression	6	1
SVE	12	2
VE	5	4
SVE/VE	5	1

**Table 9** Cardiovascular diseases in group 3 patients

Cardiovascular diseases	Quantitative assessment ( <i>n</i> = 35)	
	Number	Percentage
Postinfarction cardiosclerosis	11	31.4
FC I angina of effort	4	11.4
FC II angina of effort	7	20
FC III angina of effort	12	34.3
Ventricular extrasystole	21	60
Supraventricular extrasystole	16	45.7
Silent myocardial ischemia	4	11.4
First-degree atrioventricular block	3	10.7
Left anterior bundle branch block	2	5.7
Stage II arterial hypertension	5	14.2
Stage III arterial hypertension	13	37.1

value of the total score of the SAQ for “angina of efforts” demonstrated prior to surgery was 72.5% ± 3.1%. After TURP operation, this parameter improved to 80.7% ± 3.0% (*p* < 0.02). Nineteen patients felt better mainly in terms of four items of the SAQ: physical activity, angina stability, severity and disease perception. In four patients with angina (two of them had ST segment depression on HM and two had SVE) the ECG at control Holter monitoring remained unchanged. Neither did their

**Table 10** Dynamics of subjective and objective parameters of urination before and after operation in patients of group 3 ( $n = 35$ )

Parameters	Before treatment	After treatment	<i>p</i>
IPSS	18 (12–22)	14 (10–18)	0.0001
QoL	5 (3–6)	3 (2–4)	0.0001
$Q_{\max}$	10.5 (9.5–13.5)	12.8 (10.8–14.6)	0.0001
$Q_{\text{mean}}$	4.8 (4.2–5.3)	5.2 (4.8–6.7)	0.0001
RU	60 (45–70)	35 (25–45)	0.001

angina-related quality of life undergo significant changes.

In this group, there were no patients in whom ST segment depression or rhythm disorders coincided with the urination. Apart from the fact that urination improved in all patients of this group according to the results of subjective and objective examinations (100%), 23 of them also demonstrated positive dynamics of the Holter-derived ECG parameters. This was manifested in either disappearance of episodes of ST segment depression or their decrease ( $n = 16$ ). This was also manifested in a decrease of the absolute number of extrasystoles in seven patients (in five with VE and in two with SVE) (Table 11).

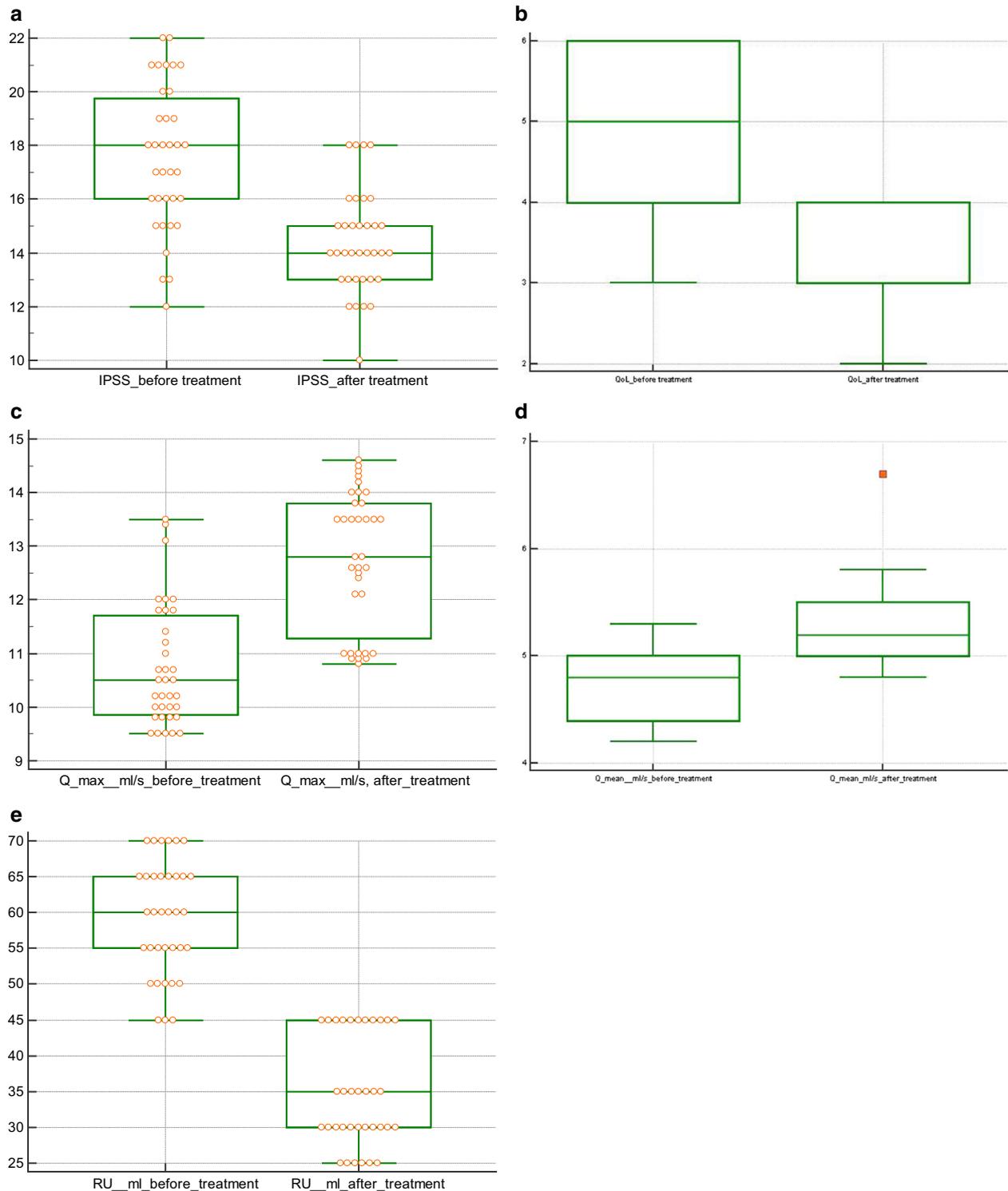
In four patients with initially present ST segment depression, the latter remained. Of these, one patient was diagnosed as having “silent” myocardial ischemia, with the remaining three patients were diagnosed as having postinfarction cardiosclerosis, functional class III “angina of effort” and arterial hypertension.

The absolute number of extrasystoles over 24 h in patients in whom their number decreased on the background of improved urination, prior to operation, did not exceed 1300. No positive dynamics of the Holter-based ECG occurred in six patients with SVE and in two with VE. The number of extrasystoles in them prior to operation was more than 1800 over 24 h. These patients had more pronounced cardiac pathology as compared with those having positive dynamics of 24-h monitoring of ECG.

## DISCUSSION

The storage and voiding LUTS due to BPH (frequent and obstructed urination in the day and night-time, feeling of incomplete bladder emptying, urgency) and psychological problems associated with this may have a negative impact on the cardiovascular system (CVS). These include cardiac arrhythmias, angina pectoris, sensation of not getting enough air, as well as cardialgias [9]. Obstructed urination, requiring additional efforts at the expense of prolonged tension of abdominal muscles, promotes increased intra-abdominal pressure, a high positioning of the diaphragm and breath holding. Impairment of a patient’s sleep and rest regimen (due to frequent diurnal and nocturnal urge to urinate) also negatively influences CVS function [9–11]. The pathogenesis of reflex changes of the CVS in patients with BPH may be presented as follows: long-standing obstruction of lower urinary tract, induced by BPH, impairs the primary afferent impulsion from the genitourinary organs. Alterations in their intramural nerve fibres and endings underlay pathological impulsion, leading to formation of dominant foci of excitation in the cortex and subcortex, particularly in the hypothalamus and reticular formation. From here, pathological impulses are transferred by efferent pathways through the underlying portions of the CNS and further through sympathetic fibres to reach vasomotor receptors of the heart. On the background of atherosclerotic alterations of the coronary vessels, an inadequate reaction may occur in the form of vascular spasm, with the development of angina and respective alterations on the electrocardiogram, as well as impaired conduction with events of arrhythmia, in particular, extrasystole [6].

Currently, depending on the indications, most patients with LUTS/BPH receive medical care in the scope of either conservative treatment (predominantly alpha-1 adrenoceptor blockers are administered) [12] or operative interventions (various modifications of transurethral endoscopic or open interventions) [13, 14]. Early adenomectomy in patients with BPH contributes to (promotes) complete



**Fig. 5** Mean value of subjective and objective parameters of urination before and after surgery (TURP) in patients of the third group: **a** IPSS; **b** QoL; **c** Q max; **d** Q mean; **e** RU

**Table 11** Predominant changes during HM and their dynamics before and after treatment of BPH in group three patients with IHD

<i>n</i> = 28	Before treatment of BPH	After treatment of BPH
ST segment depression	20	4
SVE	8	2
VE	7	5

elimination of alterations of the central haemodynamics and myocardial contractility, including normalization of arterial pressure and renin secretion [6, 9, 10, 15–20]. The obtained findings suggest that patients with prostatic hyperplasia along with irreversible alterations in the CVS also have reversible, reflex, disappearing changes after adenomectomy [5, 6, 21].

The findings of our study demonstrated that BPH-related urination disorders (LUTS/BPH) have an impact on the CVS function in patients with IHD/BPH. Holter-detected cardiac impairments in patients with IHD and BPH, especially during urination, make it possible to consider obstructive and irritative symptomatology in BPH as a factor in the additional load on the activity of the CVS. This compels us to look differently at how quality of life is affected in this cohort of patients suffering from both BPH and IHD as compared with those having either BPH or IHD alone.

According to the data of HM, at the moment of urination, 24% of patients were found to experience ischemia manifesting itself as ST segment depression and arrhythmia in the form of SVE and VE. The findings of retrospective analysis demonstrated that these alterations occurred at the height of the urge to urinate. In the majority of patients (76%) at the moment of urination and some time prior to it, negative dynamics of ECG was not revealed. Apparently, this was related to appropriately selected cardiotropic therapy or inconsiderable severity of cardiac pathology.

The alpha-1 adrenoceptor blocker tamsulosin improved the subjective and objective

parameters of urination (LUTS/BPH) in patients with IHD, as shown by the HM findings, and improved the course of IHD in 72% of patients. However, in the remaining 28% of patients the parameters of ECG after the course of treatment with alpha-1 adrenoceptor blockers do not change, despite improved urination. Apparently, this is associated with more pronounced cardiac pathology in these patients. Mention should also be made that none of our patients with IHD refused to take alpha-1 adrenoceptor blockers. They were found to have no pronounced hypotensive response, increased intensity and frequency of cardiac pain, nor cardiac arrhythmia on the background of taking alpha-1 adrenoceptor blockers.

Positive dynamics of the Holter-derived ECG 1 month after operative intervention for BPH was observed in the majority (65.7%) of patients with IHD. Negative dynamics of the Holter-based ECG was registered in none of the patients who were operated on.

In our opinion, it is also very important that restoration of normal urination is accompanied by the patient's psychoemotional background. The patient does not have to wake up in the night to urinate, thus violating his rest regimen, to worry before each urination about how the urine will pass, or to many times a day hurriedly look for a place in a public facility to relieve himself. This, without doubt, has a beneficial effect on the course of IHD in this cohort of patients.

## CONCLUSIONS

Impaired urination in LUTS/BPH patients is an additional load on the CVS and worsens the course of IHD. Holter monitoring makes it possible to identify groups of patient in whom urinary impairments caused by prostatic hyperplasia negatively affect the course of IHD. Restored urination (either conservatively or operatively) in patients with BPH in 72% of cases decreased the number of fits of angina, thus influencing favourably the course of IHD.

All the factors mentioned above should be known and taken into consideration during examination and therapeutic decision-making

in patients with IHD and LUTS/BPH by both the urologist and cardiologist.

### Limitations of the Current Study

The genetic analysis of the patients included in this study was not provided. It could be important to investigate gene abnormalities for the cardiovascular and prostate diseases. At present, the information regarding coexisting diseases in the selected patients and their previous treatment history is absent.

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**Compliance with Ethics Guidelines.** All procedures performed in the study were in accordance with standard clinical care and were in accordance with the I.M. Sechenov First Moscow State Medical University IRB and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by I.M. Sechenov First Moscow State Medical University IRB Protocol Record 03-19 and was registered on ClinicalTrials.gov (NCT03856242). Informed consent was obtained

from all individual participants included in the study.

**Data Availability.** The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

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