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Correction of the Elevated Blood Pressure in Patients Undergoing Robot-Assisted Radical Prostatectomy

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Коррекция гипертензии у пациентов при выполнении робот-ассистированой радикальной простатэктомии

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Summary

The aim of the study was to evaluate the role of urapidil hydrochloride for the management of abnormal cardiovascular response in patients undergoing robot-assisted radical prostatectomy (RARP).

Material and methods. The total of 93 prostate cancer patients scheduled for elective RARP were included and randomized in two groups: urapidil (n=44) and standard anesthesia control group (n=49). Urapidil was used to control the elevated blood pressure intraoperatively. Central hemodynamic monitoring was performed at 5 steps of the surgery.

Results. In the control group, the step 2 of the procedure was associated with elevated mean blood pressure (by 24.3%, P=0.045) and increased total peripheral vascular resistance (by 46.6%, P=0.011) compared with step 1, while in the urapidil group no significant changes in these parameters were found. In the urapidil group, the blood pressure was lower by 20.2% (P=0.047), afterload by 36.9% (P=0.02) vs the control group values, whereas the cardiac output was higher by 22.2% (P=0.043). Placing patient in the steep Trendelenburg position (step 3) resulted in a 22.4% increase in stroke volume (P=0.38) in the control group and a 19.2% increase in stroke volume (P=0.049) in the urapidil group compared with the previous step. Cardiac output in the urapidil group was higher by 34% (P=0.002) and blood pressure and vascular resistance were lower by 24.4% (P=0.031) and 45.7% (P=0.001), respectively, vs the control group. At steps 4 and 5, gradual stabilization of the hemodynamic parameters and peripheral vascular tone with significantly smaller differences between the groups were revealed.

Conclusion. Urapidil was effective for maintaining central hemodynamic parameters in patients during robotic-assisted radical prostatectomy at step 2 of the procedure, avoiding blood pressure elevation at step 3 and significantly reducing the total peripheral vascular resistance compared with the control group.

Keywords: robotic-assisted prostatectomy; steep Trendelenburg position; urapidil

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Robot-assisted radical prostatectomy (RARP) has been gradually replacing the open radical surgery and becomes the «gold standard» treatment of patients with localized prostate cancer globally. Primarily, this is due to its minimal invasiveness, better functional results (concerning urine retention and erectile function), as well as to a shorter time needed to achieve clinical success [1, 2].

CO_2 pneumoperitoneum and Trendelenburg position are prerequisites for optimal visualization of the surgical field in RARP. This combination can negatively affect both pulmonary and cardiovascular systems, which necessitates a thorough understanding of the pathophysiology involved, as well as timely feedback of function control to prevent the development of life-threatening conditions.

In addition to pulmonary dysfunction associated with atelectasis and increased airway pressure, RARP results in severe hemodynamic changes [3–6]. According to Lestar M. et al. who evaluated central hemodynamic parameters using Swan–Ganz catheter, the central venous pressure increased almost 3 times compared to the baseline with a simultaneous 2-fold increase of mean pulmonary artery pressure and pulmonary capillary pressure (P<0.01) while the patient was placed in Trendelenburg position at 45°. Meanwhile, the mean arterial pressure, increased by 35% [7].

In the study of Pawlik M. T. et al. the central hemodynamic parameters during RARP were assessed using the PICCO+ (Pulse Contour Cardiac Output with continuous measurement of cardiac output using pulse waveform analysis) invasive technique. The authors reported perioperative cardiac complications in 5.9% of patients, with 11.8% having cardiac deterioration in the intraoperative period with a significant decrease in cardiac index (up to 1.5 L/min/m^2 versus baseline of 2.6 L/min/m^2 (P=0.003)) after the CO_2 pneumoperitoneum and Trendelenburg position and an increase in total peripheral vascular resistance to 6865 dyn×s×sm^{-5} versus 2879 dyn×s×sm^{-5} at baseline (P=0.001) [8].

Thus, hypertension during CO_2 pneumoperitoneum and Trendelenburg positioning of the patient is the most significant hemodynamic complication of RARP. In this regard, studying drugs with a well-controlled hypotensive effect used as a part of anesthesia regimen seems reasonable. We believe that urapidyl hydrochloride possessing strong alpha-blocking activity perfectly meets this goal. In the available literature, we found no studies addressing pharmacological control of hypertension in RARP.

Undoubtedly, the Swan–Ganz catheter is the most objective method for assessing central hemodynamic parameters [7, 9], but due to complexity and possible complications of this invasive method, alternative noninvasive methods of hemodynamic assessment are becoming more and more popular [10, 11]. In our study we employed impedance cardiography using Niccomo® (Medizinische Messtechnik GmbH, Germany) device to assess cardiac contractility, preload and afterload.

The aim of the study was to evaluate the efficacy of urapidyl hydrochloride as a component of anesthesia support for the control of hypertension during robot-assisted radical prostatectomy.

Material and Methods

After approval by the ethical committee (decision of the ethical committee of the Federal Scientific and Clinical Center for Intensive Care and Rehabilitology No. 5/20/6 of December 23, 2020) and written informed consent, 93 patients with verified prostate cancer scheduled for RARP were included in the open randomized prospective study (see Fig.).

Criteria for inclusion were:

— age from 50 to 70 years

— anesthesia risk 1–2 according to ASA (American Society of Anesthesiologists);

— signed patient's informed consent for participation in the study.

Non-inclusion criteria were

— refusal to participate in the study / sign the informed consent;

— anesthesia risk ⩾3 ASA

— body mass index >33 kg/m^2

— chronic nonspecific lung diseases and/or 2–3 degree respiratory failure (dyspnea on moderate and mild exertion),

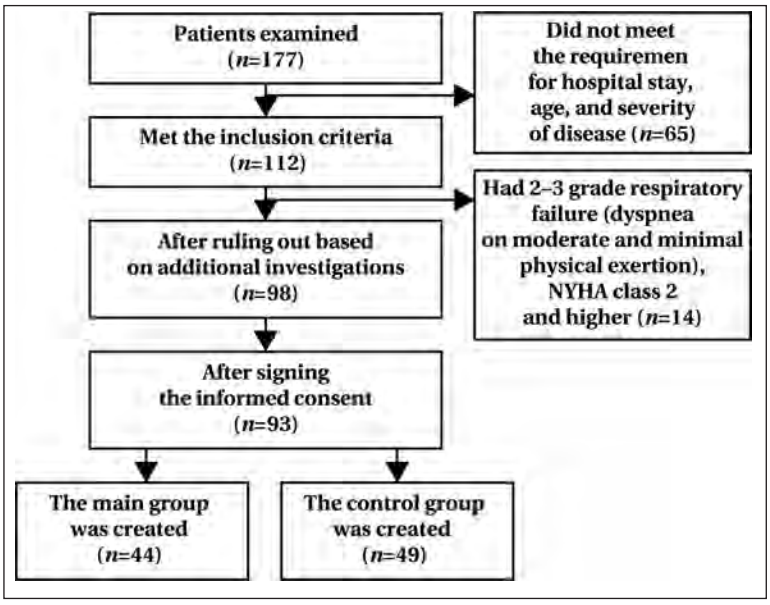

Fig. Scheme of patient recruitment.

Table 1. Characteristics of the study groups.

Parameter	Group		*P*-value
	Main (*n*=44)	Control (*n*=49)	
Age, years	57.9±0.72	57.3±0.67	0.99*
Weight, kg	74.1±2.93	73.3±2.34	0.98*
ASA	1.59±0.13	1.68±0.1	0.55**
ASA 1, % patients	38.6	32.7	
ASA 2, % patients	61.4	67.3	
Comorbidities, % of patients			
Coronary heart disease	38.6	44.9	0.32**
Chronic obstructive pulmonary disease	6.8	14.3	0.32
Gastric erosions or ulceration, remission	6.8	20.4	0.08

Note. *— Student's *t*-test; ** — χ^2 test

— chronic heart failure ⩾2 NYHA (New York Heart Association) classification.

The patients were randomized using the envelope method into 2 groups (the main and the control). The patients of the main group (*n*=44) received standard anesthesia support and intraoperative urapidil hydrochloride to correct hypertension, while the patients of the control group (*n*=49) received only standard anesthesia support. The characteristics of the groups are summarized in Table 1.

Patients aged 50–60 years prevailed in both groups. Two thirds of the patients were working at the time of diagnosis, the rest were retired. Differences in age and weight between the groups were not significant, indicating the group comparability (Table 1).

In general, the differences between the groups in the anesthetic ASA risk were not significant (Table 1).

Hemodynamic parameters were analyzed at the following key steps of surgery:

Step 0: Baseline values prior to the intervention;

Step 1: Introductory anesthesia, horizontal position of the patient;

Step 2: Induction of CO_2 pneumoperitoneum, insertion of trocars;

Step 3: Bringing the patient to the 30° Trendelenburg position, 5 min after the start of surgery with robotic assistance;

Step 4: The most invasive step of the operation, 30–60 min after the start of the intervention with robotic assistance;

Step 5: 15 minutes after tracheal extubation.

The following hemodynamic parameters were measured at each of the key steps:

— heart rate (HR), per min;

— systolic blood pressure (SBP), mm Hg;

— diastolic blood pressure (DBP), mm Hg;

— mean arterial pressure (MAP), mm Hg;

— cardiac output (CO), L/min;

— stroke volume (SV), ml;

— total peripheral vascular resistance (TPR), $dyn \times s \times cm^{-5}$.

After the patient was transported to the operating room the standard (electrocardiogram, noninvasive blood pressure measurement, pulse oximetry) and invasive (peripheral venous catheter 18G-20G inserted into a vein of the left upper extremity with the right arm adducted to the torso and fixed during the operation) monitoring were initiated. The Niccomo® device was connected as an additional monitoring component with 4 twin electrodes preoperatively placed on the neck and chest.

The dosage of drugs for combined endotracheal anesthesia was calculated based on the ideal body weight. All patients received standard pharmacological premedication on the operating table together with 100% oxygen insufflation through a face mask at 6–8 l/min consisting of 0.1% atropine sulfate 0.01–0.02 mg/kg, 0.2% clemastine (Tavegil®) 0.03–0.05 mg/kg, midazolam (Dormicum®) 0.02–0.06 mg/kg, 0.005% fentanyl 1–3 mg/kg. Induction anesthesia was initiated by injecting propofol (Diprivan®) 1.5–2.5 mg/kg until the target BIS values of 30–40 were achieved.

After achieving depressed consciousness, the precalculated dose of non-depolarizing myorelaxant rocuronium bromide 0.5 mg/kg was injected and tracheal intubation was performed with 8–9 mm endotracheal tube. Due to the risk of displacement of the distal end of the endotracheal tube toward the carina and single-lung ventilation after placing the patient in Trendelenburg position, obligatory auscultatory control was performed at all stages of patient positioning. After tracheal intubation, a nasogastric tube was placed to minimize the risk of injury to the stomach during trocar placement and to prevent postoperative nausea and vomiting. Anesthesia was maintained by sevoflurane (Sevoran®) inhalation anesthetic with the target BIS values of 40–50. Muscular relaxation was achieved by bolus injection of calculated doses of rocuronium bromide. We used Drager Primus (Dragerwerk, Germany) device for mechanical lung ventilation using oxygen-air mixture at 0.4–0.6 ratio and at a rate of 0.8–1 L/min in PCV (Pressure Control Ventilation) mode with the following parameters: respiration rate 10 per minute, respiratory volume of 6–8 ml/kg, positive end-expiratory pressure (PEEP) of 5 cm H_2O, inspiration-expiration ratio of 1:1 as the most optimal in terms of reducing the risk of lung baro-

Table 2. Hemodynamic parameters of patients from main (*n*=44) and control groups (*n*=49) during the surgery (*M*±*σ*).

Group	Baseline	Step of surgery				
		1	2	3	4	5
Heart rate, per minute						
Control	77.1±2.78	83.1±2.56	67.1±3.45*,#	65.2±2.36*	66.1±1.76*	74.2±2.3
Main	74.1±1.53	81.4±2.26	71.5±2.78*	68.1±1.78*	72.7±2.31*	80.7±3.5
Systolic blood pressure, mm Hg						
Control	125.8±2.32*	102.4±3.4	136.4±1.85*,#	141.3±2.12*	133.2±1.76	126.6±1.3*
Main	129.1±1.78*	99.4±3.2	131.5±1.6*,#	105.7±1.57*,##,#	107.1±2.14*,##	132.4±2.2*,#
Diastolic blood pressure, mm Hg						
Control	80.1±1.48	68.2±1.96	87.5±1.05*,#	92.3±1.34*	84.8±2.15	73.7±1.6
Main	83.3±2.16	72.1±1.46	70.7±1.52##	71.3±1.56##	68.6±1.75##	78.4±2.32*
Mean arterial pressure, mm Hg						
Control	95.4±1.3	80.2±1.8	99.7±1.15*,#	112.6±1.42*	102.3±2.13*	92.6±1.4
Main	91.4±1.6	84.1±1.2	79.6±2.04##	85.1±2.12##	78.7±1.67*,##	93.2±1.9*
Cardiac output, L/min						
Control	6.1±0.23	5.4±0.24	4.5±0.3	4.7±0.14	5.4±0.16*	5.7±0.23
Main	5.5 ±0.41	5.7±0.14	5.5±0.24##	6.3±0.35*,##	5.8±0.24*	5.2±0.35
Stroke volume, ml						
Control	78±2.78*	65±2.85	67±1.98	82±2.63*,#	83±3.02*	77±2.48
Main	74±3.16	71±3.65	78±2.34	93±1.87*,#	91±2.56*	75±3.13
Total peripheral vascular resistance, dyn×s/cm^5						
Control	1254±24.1	1138±29.3	1668±27.2*	1763±19.3*	1418±26.2#	1210±24.2
Main	1275±26.3	1208±24.7	1053±23.8##	957±16.7*,##	1024±20.1##	1094±17.4

Note. Significant differences: * — versus step 1, $P<0.05$, Duncan test; # — versus the previous step, $P<0.05$, Newman–Keuls test; ## — between the main and control groups, $P<0.05$, Student's *t*-test.

trauma and impaired venous return. The respiratory rate settings during anesthesia were adjusted to achieve optimal exhaled carbon dioxide partial pressure of 4.9–6.4 vol%. The constant CO_2 insufflation through robotic trocar port and its leak into the circulation were taken into account and timely adjustment of the ventilator parameters was performed to maintain normocapnia [12].

Urapidyl hydrochloride 25 mg was administered by bolus to patients in the main group at the stage of CO_2 pneumoperitoneum induction and trocar placement (step 2), with further continuous infusion through an infusion pump at a rate sufficient to maintain mean arterial pressure at 75–80% of baseline values.

During the operation, limited volumes (1–2 ml/kg/h) of balanced crystalloid solutions were infused until the urethrovesical anastomosis was created in order to limit the production and leakage of urine into the operating field, as well as to prevent impaired visualization of the area of surgical interest and reduce the likelihood of upper airway obstruction in Trendelenburg position. After the anastomosis was created, an additional 1,000 ml of balanced crystalloid solutions were administered.

The duration of surgical intervention (212.13±11.2 min for patients in the main group and 225.2±13.6 min for patients in the control group) did not differ between the groups (P=0.83, Student's *t*-test). Intraoperative blood loss was less than 100 ml in both groups. After completion, all patients underwent tracheal extubation and were transferred in stable condition to the postoperative ward for symptomatic therapy and clinical and laboratory monitoring. Both groups did not differ statistically in an average hospital stay which was 7±1 days.

The RARP was performed using da Vinci Si system (Intuitive Surgical, Mountain View, USA). After tracheal intubation, the patient was placed in the lithotomy position; special soft fixators were positioned under the patient's shoulders to limit his/her displacement relative to the operating table. Five ports were inserted into the abdominal cavity creating CO_2 pneumoperitoneum with initial CO_2 pressure of 15 mm Hg. After this step was completed and the patient was moved to Trendelenburg position, gas pressure in the abdominal cavity was reduced to the safe 12 mm Hg [6, 9, 13].

Considering the exploratory nature without a primary endpoint, the sample size of the study was not specified. Ninety-three patients were considered suitable for analysis of hemodynamic parameters during RARP. The quantitative data distribution was checked for normality using the Shapiro–Wilk criterion. Taking into account normal distribution of the data, statistical variables were presented as mean values (*M*) with standard deviations (σ). Comparison between the groups was performed using Student's *t*-test. Statistical differences between the mean values in the groups at different steps of the surgery were assessed by univariate analysis of variance (Newman–Keuls criterion for comparison with the same parameter's value at the previous stage and Duncan criterion for comparison with the value of step 1). Pearson's χ^2 test was used to compare frequencies, Yates' correction was applied for expected frequencies less than 10, and Fisher's exact test was additionally calculated for expected fre-

quencies less than 5. Statistical analysis was performed using Statistica 10.0 software package. Differences were considered significant at $P<0.05$.

Results and Discussion

The baseline hemodynamic parameters remained within the reference range (Table) due to premedication with sedatives and a conversation with an anesthesiologist with a detailed description of upcoming events held the day before, which reduced the impact of the emotional component on hemodynamics. After induction anesthesia, mean arterial pressure (MAP) values decreased insignificantly in both groups, remaining within the target values, ensuring adequate microcirculation.

During step 2, where the installation of ports and the induction of CO_2 pneumoperitoneum (with CO_2 pressure -– mmHg) occur, the control group demonstrated cardiovascular changes including an increase in SBP (33.2%, *P*=0.037), DBP (28.3%, *P*=0.041), MAP (24.3%, *P*=0.045), and vascular resistance (46.6%, *P*=0.011), as well as a slight 16.7% decrease in cardiac output (*P*=0.61) versus step 1. The CO_2 pneumoperitoneum obviously had a strong stressful effect on the cardiovascular system, which necessitated additional doses of opioid analgesics at this step. Falabella A. et al. and Meininger D. et al. in their studies obtained similar results [14–16].

In the main group, MAP and TPR decreased by 5.4% (*P*=0.62) and 12.8% (*P*=0.092), respectively, during step 2 compared to step 1.

The DBP in the main group was 19.2% (*P*=0.049) less than in the control group, as were MAP (20.2%, *P*=0.047) and TPR (36.9%, *P*=0.02), while the CO was 22.2% (*P*=0.043) higher versus the control group.

Patient's placement in Trendelenburg posotion (step 3) led to a 22.4% increase in stroke volume (*P*=0.038) and an insignificant increase in MAP (12.9%, *P*=0.62) and afterload (5.7%, *P*=0.83) in the control group vs with the previous step, which is likely due to the increased venous return to the heart as a result of elevation of the lower extremities, increased intra-abdominal pressure and sympathetic activation [8]. These findings agree with the data obtained in the study of Rosendal C. et al. who found a significant increase in TPR at all steps of RARP and its reduction below the baseline values only at the end of the surgery [15].

In the main group, a 19.2% increase in stroke volume (*P*=0.049) and a 19.6% decrease in SBP (*P*=0.049) were revealed at the step 3 vs the previous step. Increases in cardiac output by 14.5% (*P*=0.61) and MAP by 6.9% (*P*=0.23) and a 9.1% decrease in afterload (*P*=0.12) were not significant compared with the previous step.

The CO in the main group was 34% higher vs the control group (*P*=0.002), and MAP and TPR were 24.4% (*P*=0.031) and 45.7% (*P*=0.001) lower, respectively. The stroke volume in the main group was insignificantly higher (13.4%, *P*=0.13) relative to the control group.

The hemodynamic parameters were stable during step 4, which is the most invasive part of the surgery with separation of the seminal vesicles, dissection of the dorsal venous complex and removal of the prostate, followed by urethrovesical anastomosis. Interestingly, the SBP was 24.4% (*P*=0.035) lower in the main group, DBP was 23.6% (*P*=0.039) and MAP 30% (*P*=0.004) lower than in the control group. The TPR was insignificantly lower vs the control group (27.8%, *P*=0.12), while the SV and CO were 9.6% (*P*=0.51) and 7.4% (*P*=0.73) higher, respectively.

Lestar M. et al. and Falabella A. et al. reported similar results in their research [7, 16]. Several studies have demonstrated wide variation of SV and CO changes, from an 11% decrease to significant increase (more than 20%) at the same step of the operation [17, 18].

The final step of the study was characterized by the return of most of the studied parameters to their baseline values in both groups. Only DBP and SV in the main group remained slightly decreased vs the step 1, which was probably caused by limited intraoperative infusion of crystalloids due to the specific nature of the surgery. In the postoperative room, the volume status was corrected in all patients using balanced crystalloid infusion [16].

Thus, the use of urapidyl hydrochloride during anesthesia support in RARP allowed to stabilize hemodynamic parameters at step 2 of surgery, to avoid hypertension at step 3, and to significantly reduce the afterload.

A more stable hemodynamic profile in the patients of the study group during critical stages of surgery such as induction of CO_2 pneumoperitoneum and patient placement into the Trendelenburg position can be suggested [19–22].

Another important effect of urapidyl hydrochloride during anesthesia in RARP was the reduced frequency of «critical» hemodynamic accidents during the surgery. Thus, significant hypertension (more than 40% increase in BP vs the step 1 values) was observed in 25 (51.0%) patients in the control group, while only 3 (6.8%) patients had a similar response in the main group (*P*=0.00001). A significant decrease in CO was seen in 8 (16.3%) patients of the control group, while in the main group this was found only in 1 (2,3%) patient (*P*=0.033). Also, 6 (12.2%) patients in the control group experienced a significant increase in TPR, while in the main group no similar increase in afterload was found (*P*=0.028).

Conclusion

The use of urapidyl hydrochloride as a part of anesthesia support to control the hyperdynamic

cardiovascular response allows to achieve the target MAP values during all steps of surgery by reducing the afterload and maintaining the heart performance without reducing organ and tissue perfusion and compromising the cardiovascular adaptive response.

The use of urapidyl hydrochloride ensures stability of hemodynamic parameters during the whole intraoperative period, which contributes to the adequacy and safety of anesthesia and can be crucial in patients with cardiovascular comorbidities.

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