# Quantitative Evaluation of Upper Urinary Tract Pump Function in Pigs With Acute Unilateral Lower Ureteral Obstruction by 640-slice Dynamic Volume CT

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**Research Article**

**Keywords:** Urethral obstruction, Dynamic volumetric CT, Renal pelvis constant pressure perfusion test, Upper urinary tract urodynamics, Pump function

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**Quantitative evaluation of upper urinary tract pump function in pigs with acute unilateral lower ureteral obstruction by 640-slice dynamic volume CT**

**Running title:** 640-slice DVCT in evaluating ureteral obstruction

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**Abstract**

**Background:** It is a challenging problem to differentiate obstructive hydronephrosis from non-invasive evaluation of renal pelvis and ureteral motility in patients. The purpose of this study was to explore the value of 640-slice dynamic volume CT (DVCT) in quantitative measurement of upper urinary tract (UUT) pump function after acute unilateral lower ureteral obstruction in pigs.

**Methods:** In this study, perfusion pig model was made by constant pressure perfusion test of renal pelvis and left nephrostomy. The perfusion and pressure measuring devices were connected to create the state of no obstruction, acute obstruction of the lower part of the left ureter. After successful modeling, continuous dynamic volume scanning of bilateral renal excretion phase was performed with 640-slice DVCT, and pump functions of the renal pelvis and part of the upper ureter were calculated and analyzed. No obstruction, acute obstruction of the lower part of the left ureter. Pump functions of the renal pelvis and part of the upper ureter.

**Results:** Results showed after LUUT fistulostomy, the time difference between the average UUTs volume and positive volume value increased gradually, and the calculated flow velocity decreased, which was significantly different from that of the RUUT. The volume difference of the LUUT increased significantly in mild obstruction. In the bilateral control, the volume change rate of the LUUT increased in mild obstruction and decreased in severe obstruction, and there was significant difference between the left and the right side.

**Conclusion:** The continuous dynamic volume scan and measurement of 640-slice DVCT can obtain five pump function data of UUT in pigs with acute lower ureteral obstruction.

**Key words:** Urethral obstruction; Dynamic volumetric CT; Renal pelvis constant pressure perfusion test; Upper urinary tract urodynamics; Pump function

## Background

It is a challenging problem to differentiate obstructive hydronephrosis from non-invasive evaluation of renal pelvis and ureteral motility in patients with obstructive and non-obstructive hydronephrosis[1]. Because at present, the evaluation of urodynamics of the upper urinary tract in clinical work mainly depends on non-invasive imaging examinations, such as ultrasound, intravenous pyelography, CT, MRI [2], radionuclide and dynamic near infrared fluorescence imaging [3], and these imaging methods speculate the functional changes of the upper urinary tract based on the morphological changes of the upper urinary tract, and only some semi-quantitative data have been obtained [4, 5]. The clinical quantitative evaluation of upper urinary tract urodynamics still depends on the classical upper urinary tract urodynamic tests, that is, renal pelvis constant pressure perfusion test and renal pelvis constant flow perfusion pressure test (Whitaker test) [6]. However, because the above two tests are invasive tests, they are only used in patients with nephrostomy [7].

In this experiment, the pig model of constant pressure renal pelvis perfusion (CPP) was established, and the upper urinary tract under different conditions of lower ureteral obstruction was scanned by 640-slice dynamic volume CT scanning technique, and the later data were calculated and analyzed to obtain the change rule of pump function of upper urinary tract under different obstruction conditions, in order to obtain the imaging method of non-invasive quantitative evaluation of upper urinary tract urodynamics instead of CPP experiment. It is expected to replace the renal pelvis constant pressure perfusion test as an effective method for non-invasive quantitative imaging evaluation of UUT urodynamics.

## Methods

### Animals

Experimental animal modeling and grouping healthy Diannan small-eared pigs are provided by the Experimental Animal Department of Kunming Medical University (Experimental Animal license No.: SYXK (Yunnan). Ten pigs, weighing 25 kilograms and half male and female, are raised by the Experimental Animal Center of Kunming Medical University. the feeding conditions are: room temperature (21℃, air humidity 50% 60%, light changes naturally with day and night, and enter the water freely. The kidneys of 10 pigs were divided into the left urinary tract as the experimental group and the right urinary tract as the control group. The process of this experiment is in accordance with the regulations (Ministry of Science and Technology of the people's Republic of China, guidance on being kind to Experimental Animals, 2006-09-30), and has been approved by the Medical Ethics Committee of Kunming Medical University.

### Nephrostomy

Before anesthesia, all experimental pigs fasted drinking and fasting 12 hours before the experiment, intraperitoneal injection of 3% pentobarbital sodium 10mg / kg, establishment of ear vein channel and maintenance of intravenous infusion after successful induction of anesthesia, tracheal intubation and connection of ECG monitor, etc. The initial dose of 3% pentobarbital sodium 7.2mg/kg (administration rate 1~2ml/min) was given. According to the anesthetic condition of the animal (such as restlessness, pain reaction, etc.), the initial dose of 30min was increased by 1 minute, 4 cycles, 1 stroke, 3. After successful anesthesia, fix the pig in the right lying position, take the left subcostal incision, cut open the muscle layer and peritoneum with an electric knife, expose the left kidney, find and separate the left ureter on the anterior medial and inferior side and in front of the psoas major muscle, retain the upper segment of the ureter 3mur4cm, keep the ureter and renal hilum in a straight line, and use a catheter sheath to protect 0.035 hard guide wire retrograde into the renal pelvis from the ureteral incision and out of the kidney. The wound of renal cortex was enlarged with the tip of catheter sheath and then withdrawn. Then insert the F8 fistulostomy tube, the length of the fistulostomy tube is 15cm, pull the guide wire to send the fistulostomy tube into the renal pelvis, the operator touches the tube head in the renal pelvis and fix it. Put the F12 suction tube on the control valve and insert it into the upper ureteral stump, the distal end of the tube is more than 3cm from the ureteropelvic junction, the distal end is drawn out of the body and connected to the urine bag, and a catheter is inserted into the lower ureteral stump on the left to drain bladder urine. After fixing the position of the left nephrostomy tube and catheter, the kidney was taken back, the bleeding was stopped thoroughly and the abdominal cavity was closed layer by layer with suture, and the incision was closed with film dressing.

**Perfusion**

Establish tee for left kidney CPP test to connect manometer tube, perfusion tube and fistulostomy tube, all tubes are fully vented, scan is image observation to ensure no bubble interference, the perfusion tube and manometer tube are suspended on the infusion rack, and the liquid level height of the manometer tube and perfusion tube is 20cm (20cmH20) above the renal pelvis plane (marked as 0 scale). The perfusion solution is a mixture of iodopropamide saline solution (10%), and a small amount of methylene blue is added for easy observation; the perfusion tube and the manometer tube are modified with the same type and length of blood vessels (Figure 1).

**Detection**

The control valve of the drainage tube at the upper end of the left ureter was set to 100,50 and 25% open at an interval of 30 minutes respectively, and the ureter was made into a non-obstruction, mild and severe obstruction state and scanned by CT. In the experiment, adjust the height of perfusion solution to control the constant perfusion pressure. Measure the amount of liquid flowing out of 1cm when the perfusion fluid height decreases, then each time the liquid is removed, the perfusion bottle will be raised by 1cm to maintain a constant pressure. After the beginning of constant pressure perfusion, the perfusion velocity has a process of first fast, then slow, then slightly faster and finally to steady, which lasts for 5 to 10 minutes, so the flow velocity is recorded 10 minutes after the beginning of perfusion, and then CT scan is performed. Set the left ureteral obstruction state to measure the flow rate under the constant pressure perfusion of the left renal pelvis, set the control valve to 100% open, when the flow rate is more than 10ml/min (0.166ml/s), it is non-obstructive state; set the control valve to 50% open state, and measure the mild obstruction state when the flow rate is 4~10ml/min (average about 0.116ml/s); The control valve is set to 25% open, and the flow rate is less than 4ml/min (0.067ml/s) for severe obstruction [8]. The bilateral kidneys and upper ureter of pigs were scanned by volume enhancement respectively when the flow velocity was stable in the state of no obstruction, mild obstruction and severe obstruction. Scanning methods: continuous dynamic volume scanning was performed. The auricular vein was injected with 30ml Nonionic contrast agent iopramine (370mgl/ml) at the speed of 3.5ml/s with a double-barrel high pressure syringe (OptivantageHD), and then 20ml saline was injected at the same flow rate. Wait for 6 minutes after injection of contrast agent, and trigger the scanning program after entering the excretion period. Scanning parameters: tube voltage 80kV, tube current 100mAs, rotation time 0.5s, collimation 0.5mm × 320mm, scan thickness 0.5mm, scan interval 2s, a total of 10 scans. The examination bed was not moved during scanning, and 10 consecutive groups of volume images with an interval of 2s during excretion of double kidneys and upper ureter were obtained.

### Imaging

Image post-processing and subjective evaluation of image quality the original volume data of 10 groups of kidney and upper ureter obtained by 640-slice dynamic volume CT scan were imported into Vitreafx workstation (Vitreafx, Version 4.60) for post-processing operation. The volume data of renal pelvis and part of upper ureter were obtained by setting the unified CT value of interest, as shown in Figure 2. In the 10 groups, the development of the renal pelvis and upper ureter was good, part of the anatomical details were not clear, and there could be local artifacts but did not affect the volume calculation.

### Data processing

All images were analyzed and measured under the guidance of two experienced radiologists. The pump function values of left and right renal pelvis and upper ureter were measured respectively: the average volume of contrast medium (ml), volume difference (ml), time difference (s), volume change rate (%) and urine flow rate (ml/s) were calculated in all renal pelvis and renal calyx and part of upper ureter (above the lower pole plane) in each scanning field for 3 times.

The formula is as follows:

$$\text{Volume average} = \frac{\text{Sum of continuous multi} - \text{phase volume values of ipsilateral urinary tract}}{\text{Number of periods}} \quad (\text{ml})$$

$$\text{Volume difference} = \text{The maximum value of volume data obtained by multiple collection of ipsilateral urinary tract} - \text{Minimum value} \ (\text{ml})$$

$$\text{Time difference} = \text{The maximum time point in the volume data obtained by multiple collection of ipsilateral urinary tract} - \text{Minimum point in time} \ (\text{s})$$

$$\text{Volume change rate} = \frac{\text{Ipsilateral volume difference}}{\text{Average volume of ipsilateral side}} \times 100\%$$

$$\text{Calculate the flow rate of urine} = \frac{\text{Ipsilateral volume difference}}{\text{Ipsilateral time difference}} \text{（ml/s）}$$

The average values of 3 times measured by 2 physicians were recorded and calculated. At the same time, the urine flow velocity（ml/s） of drainage to the end of urine bag was recorded when the left ureter formed non-obstruction, mild and severe obstruction.

**Statistical analysis**

All data were analyzed by SPSS 23.0 statistical software. Calculate the mean and standard deviation of all values on one side. The groups were divided into two groups according to left and right, paired sample t test was used for the comparison of normal distribution, and paired rank sum test was used for the comparison of skewness distribution, and the difference was statistically significant ($P < 0.05$).

**Results**

Among the 10 pigs, 2 pigs could not be studied because of the failure of left nephrostomy. The experimental results of 8 pigs were introduced in this paper.

The data of urine flow velocity from the upper ureteral stump to the urine bag of 8 pigs were recorded, which showed that the urine flow velocity of CCP test decreased linearly in normal and different obstructive states, which met the requirements of CCP test.

Three groups of different obstruction on the left and right sides of the experimental group and the control group pump function parameters are in line with the normal distribution, using paired T-test analysis, the statistical results are as follows: Figure 3-8.

**Discussion**

**Imaging examination of urodynamics of upper urinary tract**

Urinary tract dilatation does not necessarily have obstruction, and diagnostic methods that depend on renal function may lead to misdiagnosis [7pc9]. The conventional imaging methods are static imaging, and the functional changes are inferred according to the morphological changes of the upper urinary tract [9]. For some unexplained urinary tract dilatation, it is often difficult to judge the urodynamics accurately, but it is the focus of urologists. Therefore, the previous urodynamic experiments of upper urinary tract, that is, renal pelvis constant pressure perfusion test and renal pelvis constant flow perfusion pressure measurement, were used to study and judge the urodynamics of upper urinary tract. Among them, the constant pressure renal pelvis perfusion test (CPP test) is to analyze and study the relationship between the flow rate and pressure of the upper urinary tract [7]. The perfusion fluid pressure is kept constant and the speed of the liquid passing through the upper urinary tract is measured to determine whether there is upper urinary tract obstruction or not. if the 20cmH2O pressure perfusion is used and the flow rate is less than 10ml / min, the upper urinary tract obstruction is considered. If the flow rate is always less than 4ml pinch min, the obstruction is severe, and the flow velocity is mild obstruction in 4~10ml/min [8].

This experimental method is a quantitative study, but this experiment is an invasive examination for patients with urinary tract dilatation without the need for nephrostomy, which is the main reason to limit the clinical application of this classical experiment. Lovasz S et al have verified the authenticity and accuracy of the results of upper urinary tract urodynamic diagnosis by nephrostomy patients, and tried to improve the experimental method of upper urinary tract urodynamics [10], but still invasive examination has not been widely used in clinic. Therefore, in this study, the experimental animals were modeled according to the classical CPP test, and the multi-phase volume data were collected and calculated by 640 layers of DVCT, in order to find a non-invasive quantitative research method of urodynamics of upper urinary tract.

**Analysis of urodynamic parameters of upper urinary tract in this experiment**

The perfusion pressure chosen to keep constant in this study was 1.96Kpa (20cmH2O), which was slightly higher than that of human renal pelvis pressure 0.98kpa (10cmH2O). However, under this perfusion pressure, the urodynamic parameters of the upper urinary tract did not change abnormally, indicating that this pressure was within the safe pressure range of renal pelvic perfusion and was significantly lower than the clinically accepted safety pressure of renal pelvis perfusion during percutaneous nephroscopic surgery (30mmHg) [11]. Second, because the experimental site is located in Kunming (latitude 25 °02: 11\ "north, longitude 102 °42: 31\" east, the average altitude is about 1891 m), the background altitude is high and the atmospheric pressure is low, so the standard pressure reference value of 1.96Kpa is adopted.

There is a certain resistance of the left nephrostomy tube itself, the resistance of the pipe is positively correlated with the length of the tube, and inversely correlated with the diameter of the tube. The resistance caused by the thin and long tube is greater. Therefore, if we want to reduce the influence on the perfusion experiment, we should choose the pipe with larger diameter and shorter length. Before the formal implementation of this experiment, the tubes with different diameters were selected for puncture fistulostomy of pig kidney. it was found that the larger the diameter of fistulostomy was, the more serious the damage to renal parenchyma was, and the larger the diameter of the tube was, the easier it was to cause renal parenchyma rupture. For this reason, combined with the experience of ItohK [12], the catheter of F8 was finally selected to cut its length to the outside body, and a number of side holes were made at the end of the tube at the same time to reduce the resistance of the tube.

The dynamics of upper urinary tract can be affected by bladder filling state [13]. In the case of non-diuresis or low urine flow, the filling state of the bladder will not affect the pressure in the renal pelvis, but it will affect the peristaltic frequency of the renal pelvis and ureter and accelerate its frequency, while in high urine flow or in the constant pressure renal pelvis perfusion test, bladder filling will increase the renal pelvis pressure, resulting in a significant slowdown in the speed of urine passing through the upper urinary tract. Therefore, in this experiment, the drainage tube was placed into the bladder through the distal stump of the left ureter to drain the urine in the bladder, thus eliminating the influence of the filling state of the bladder on the experimental results.

The measured urine flow rate of the left upper ureteral stump and the calculated urine flow velocity of the left upper urinary tract decreased with the change of the state of obstruction, and there was no statistical difference, indicating that the experimental fistulostomy had no definite effect on the experimental results. The follow-up data measurement is reliable.

**Comparison and analysis of functional parameters of upper urinary tract pump among groups**

The function of the renal pelvis and ureter is to transport urine from the kidney to the ureter and into the bladder for storage until urination. The body works together through a series of mechanisms to achieve this goal. The basic process of regulating ureteral peristalsis is myogenic, initiated by active pacemaker cells located in the renal pelvis, and contractile impulses are transmitted from one ureteral cell to another, making the whole ureter work as a functional complex. push the diaper into the bladder. Although the physiology of the urinary tract, particularly the pelvis and ureter, has a history of nearly 100 years of electrical activity and contractile activity. The most important of these are hydrodynamic factors, such as urine flow rate, which determine the size and pattern of urine pills, which in turn affect the changes of hydrodynamic factors such as peristaltic rhythm, velocity, amplitude and baseline pressure [1]. As early as 1979, Olsen PR believed through animal experiments that renal pelvis pressure, renal pelvis volume and ureteral peristaltic frequency were important characteristics of upper urinary tract urodynamics [14]. Referring to the definition of cardiac pump function, the important characteristics of upper urinary tract urodynamics are named "upper urinary tract pump function value" in this experiment, including the average volume value of renal pelvis and upper ureter ((ml)), volume difference ((ml)), time difference (s) corresponding to the difference, volume change rate (%) and calculation of urinary flow velocity, which can be used to quantitatively evaluate the urodynamics of upper urinary tract.

The results showed that the renal pelvis and ureter dilated in the early stage of upper urinary tract obstruction, and the hydronephrosis of renal pelvis and ureter became more obvious with the deepening of upper urinary tract obstruction. After left nephrostomy, the average volume of non-obstruction group, mild obstruction group and severe obstruction group gradually increased, and there were significant differences between mild and severe groups and right upper urinary tract. It is proved that the average volume shows the urine volume of the renal pelvis and upper ureter, which can quantitatively reflect the degree of dilatation of the renal pelvis and upper ureter.

Mudraya, I S et al found that the intermittent change of the contraction frequency of the renal pelvis is related to the change of the contraction amplitude[15]. The results of this experiment show that when the upper urinary tract is slightly obstructed, the renal pelvis and the upper part of the ureter dilate slightly and stimulate the renal pelvis and ureter to increase their contraction and peristalsis to resist the obstruction, so that the contraction frequency of the renal pelvis and ureter smooth muscle is weaker than that of the normal state, but the contraction intensity is increased. Among them, the increase of contraction showed that the difference of volume positive value was significantly larger than that on the right side, while the volume change rate was slightly higher than that on the right side. The decrease of systolic frequency is shown by the increase of time difference, but due to the limitation of obstruction, the actual pumped urine volume is accumulated in the further dilated urinary tract, which is characterized by the decrease of urine flow rate. With the further aggravation of urinary tract obstruction, the renal pelvis and upper ureter were further dilated, resulting in overload of smooth muscle tissue, further decrease in contraction frequency and weakening of contraction strength of smooth muscle. The weakening of contraction intensity showed that there was no difference between the positive value difference of volume and that of the right side, while the volume change rate was significantly lower than that of the right side, showing ineffective contraction, resulting in a significant decrease in calculated flow velocity. The decrease of contraction frequency is shown by the further increase of time difference. The results of this experiment proved the morphological and functional changes of urinary tract caused by hydronephrosis after obstruction, which was consistent with the results reported by TilligB et al. [16].

In this study, the porcine kidney was scanned by 640-slice DVCT during excretory phase, and the scanned images were segmented by Vitreafx workstation to get the volume images of renal pelvis and upper ureter. Then the volume of upper urinary tract was measured by workstation, and the specific values were obtained, thus the urodynamics of upper urinary tract was evaluated accurately. Combining the CPP experiment, one of the classical experiments of upper urinary tract urodynamics, with 640 layers of DVCT, more abundant and practical data of renal pelvis and ureteral pump function were obtained than the CPP experiment, which is an improvement and innovation of the traditional CPP experiment.

However, there is still some limitations in our study. Because this study is a large animal experiment, the experimental tissue is difficult, so the sample size is small; at the same time, the normal state, mild obstruction state and severe obstruction state of the upper urinary tract are made on the same sample in turn, which may lead to interference between each other. Despite all this, the examination methods and calculation results of this experiment have been applied to patients with urinary calculi through the ethics committee of our hospital to obtain satisfactory results.

**Conclusions**

In conclusion, our study showed that the continuous dynamic volume scan and measurement of 640-slice DVCT can obtain five pump function data of UUT in pigs with acute lower ureteral obstruction. It may replace the renal pelvis constant pressure perfusion test as an effective method for non-invasive quantitative imaging evaluation of UUT urodynamics.

**Declarations**

**Funding**

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**Competing interests**

The authors declare that they have no competing interests.

**Ethics approval**

The process of this experiment is in compliance with the ARRIVE guidelines, and has been approved by the Medical Ethics Committee of Kunming Medical University.

**Consent to participate**

Not applicable

**Consent for publication**

Not applicable

**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Code availability**

Not applicable

**Acknowledgement-**

Not applicable

**Authors' contributions**

C.M conceived, designed, and performed the experiments. C.P, S.L, L.C collected the data. M.Y, K.F, S.X analyzed the data. Y.S drafted or revised the manuscript. All authors approved the final version of this manuscript.

**List of abbreviations**

DVCT, dynamic volume CT; UUT, upper urinary tract; CPP, constant pressure renal pelvis perfusion.

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**Figure legends**

Figure 1 Model of animals receiving perfusion.

Figure 2 Volume data of renal pelvis and upper ureter interested involved in CT detection.

Figure 3 Comparison of left urinary tract calculation and measured velocity

Figure 4 Comparison of mean upper urinary tract volume between different groups

Figure 5 Comparison of extremum differences of upper urinary tract volume between different groups

Figure 6 Comparison of upper urinary tract volume change rates among different groups

Figure 7 Comparison of calculated flow rates in the upper urinary tract between different groups

Figure 8 Comparison of time differences between extremum of upper urinary tract volume between different groups

# Figures

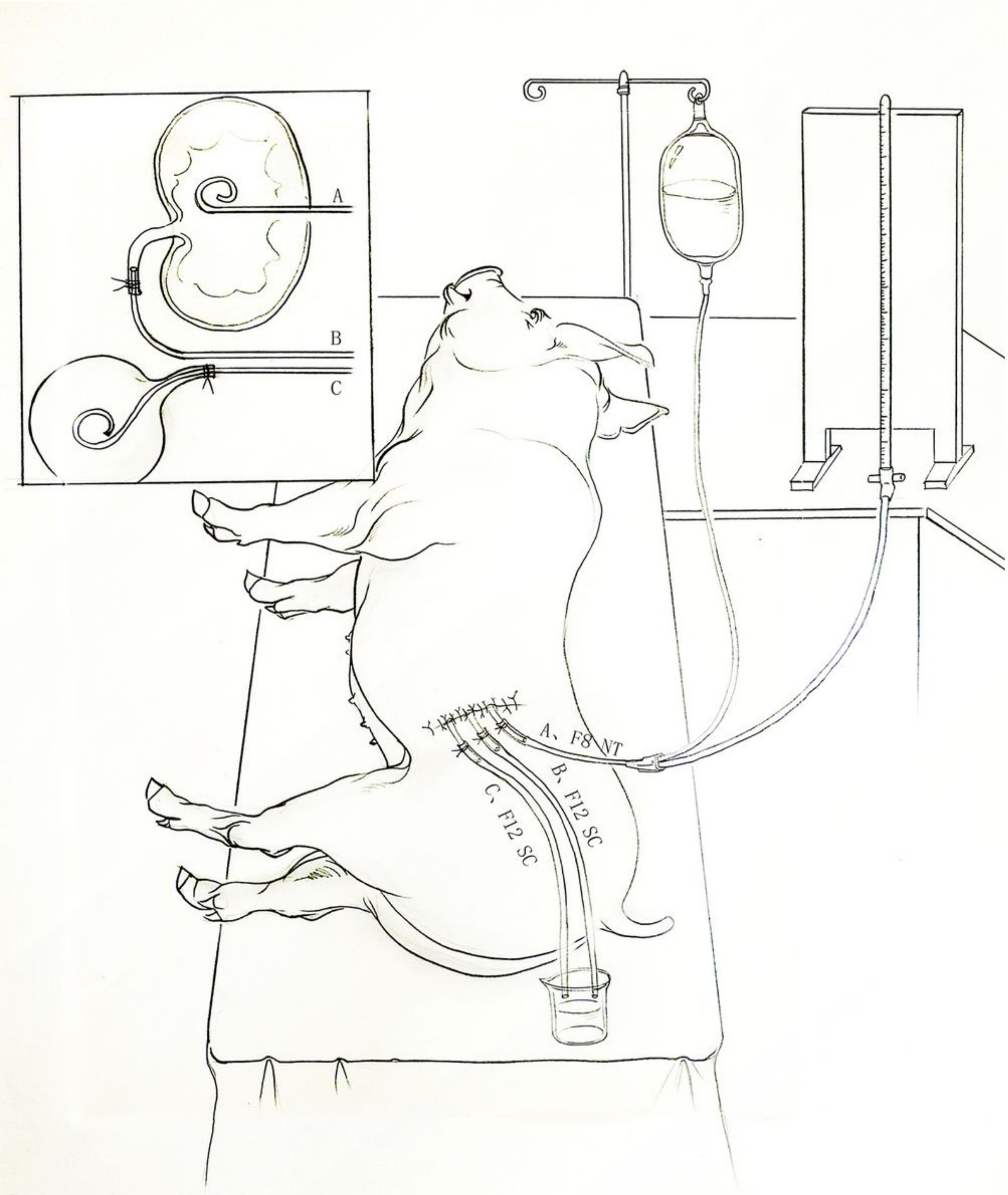


**Figure 1**

Model of animals receiving perfusion.

**Figure 2**

Volume data of renal pelvis and upper ureter interested involved in CT detection.

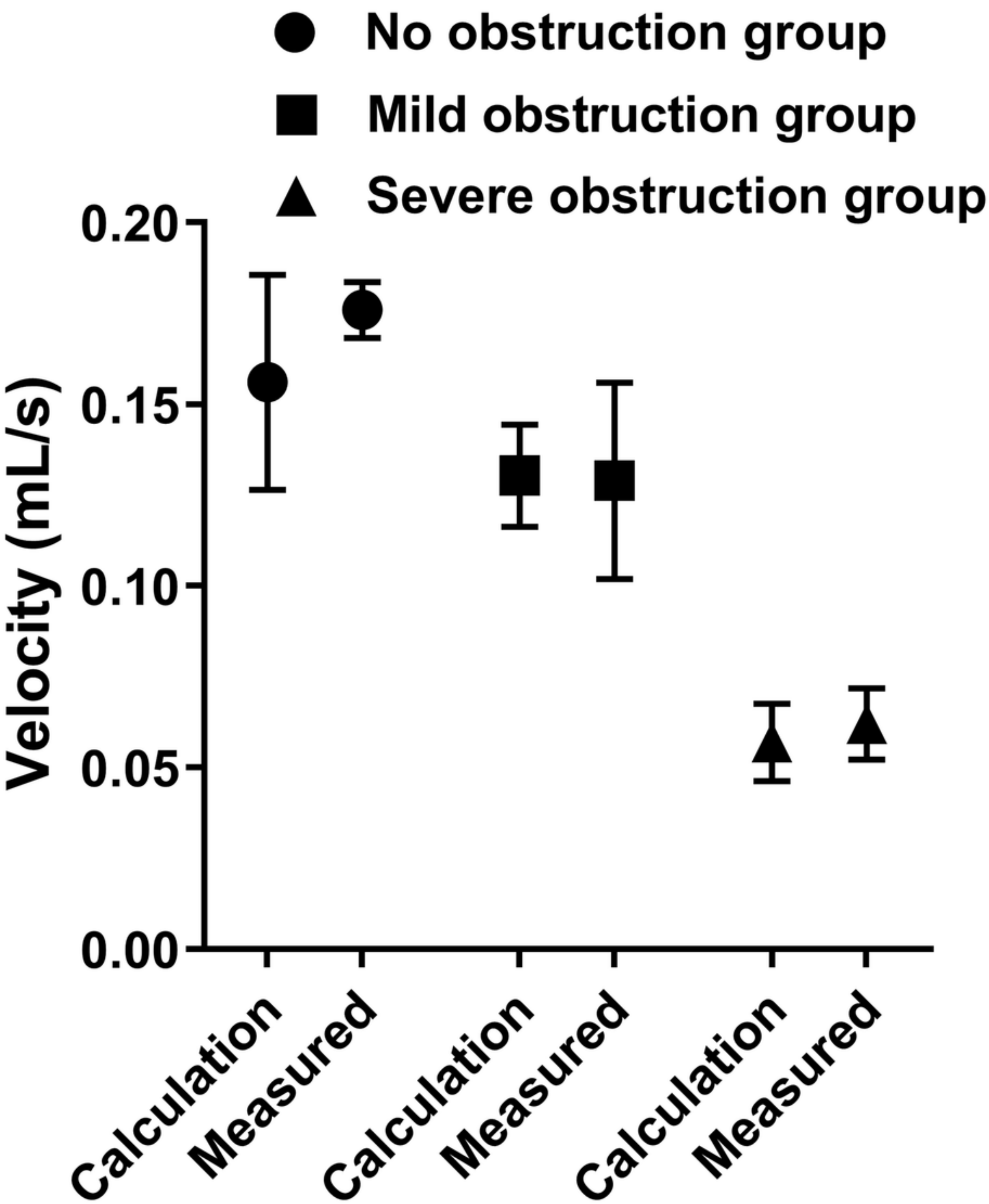


Figure 3

Comparison of left urinary tract calculation and measured velocity

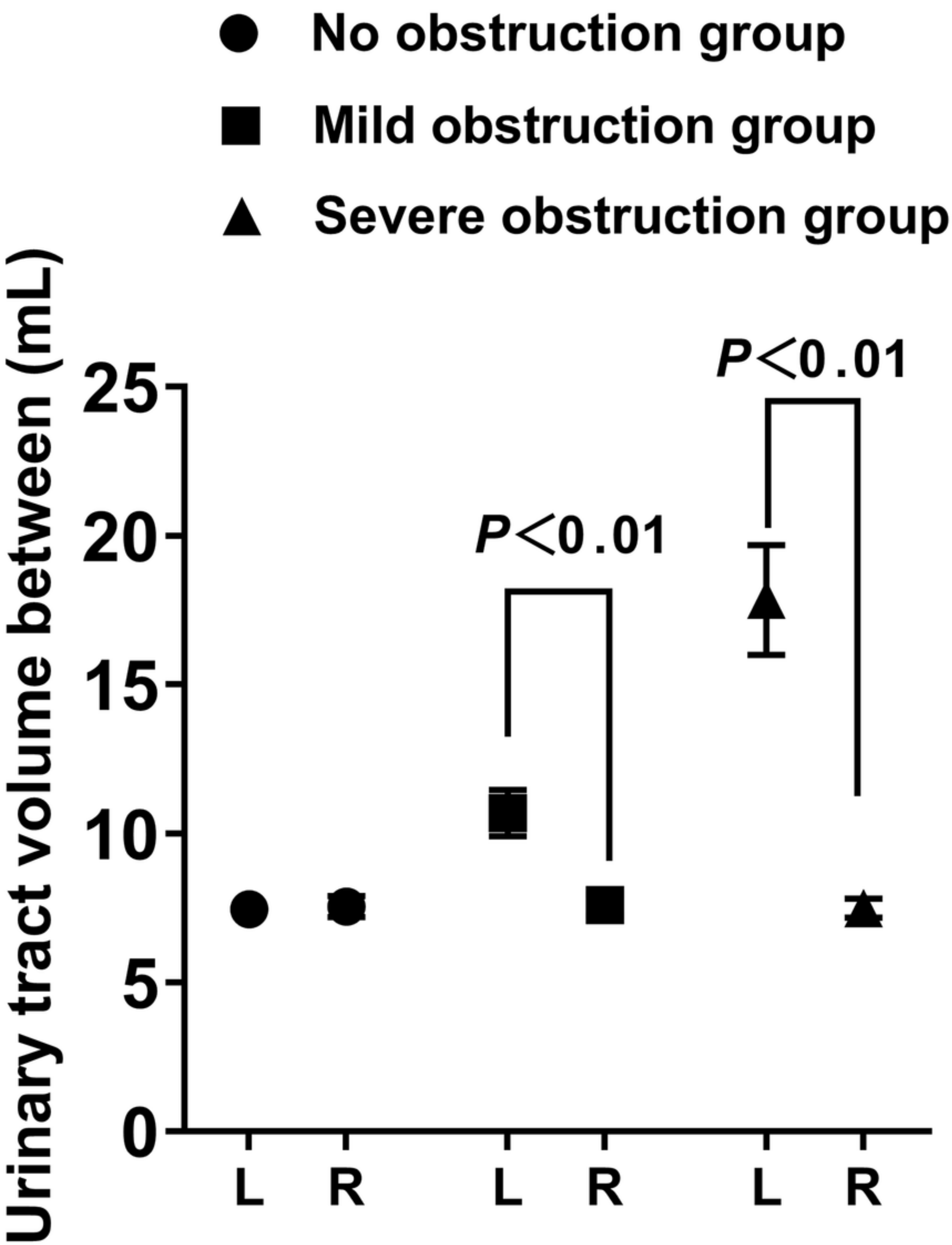


Figure 4

Comparison of mean upper urinary tract volume between different groups

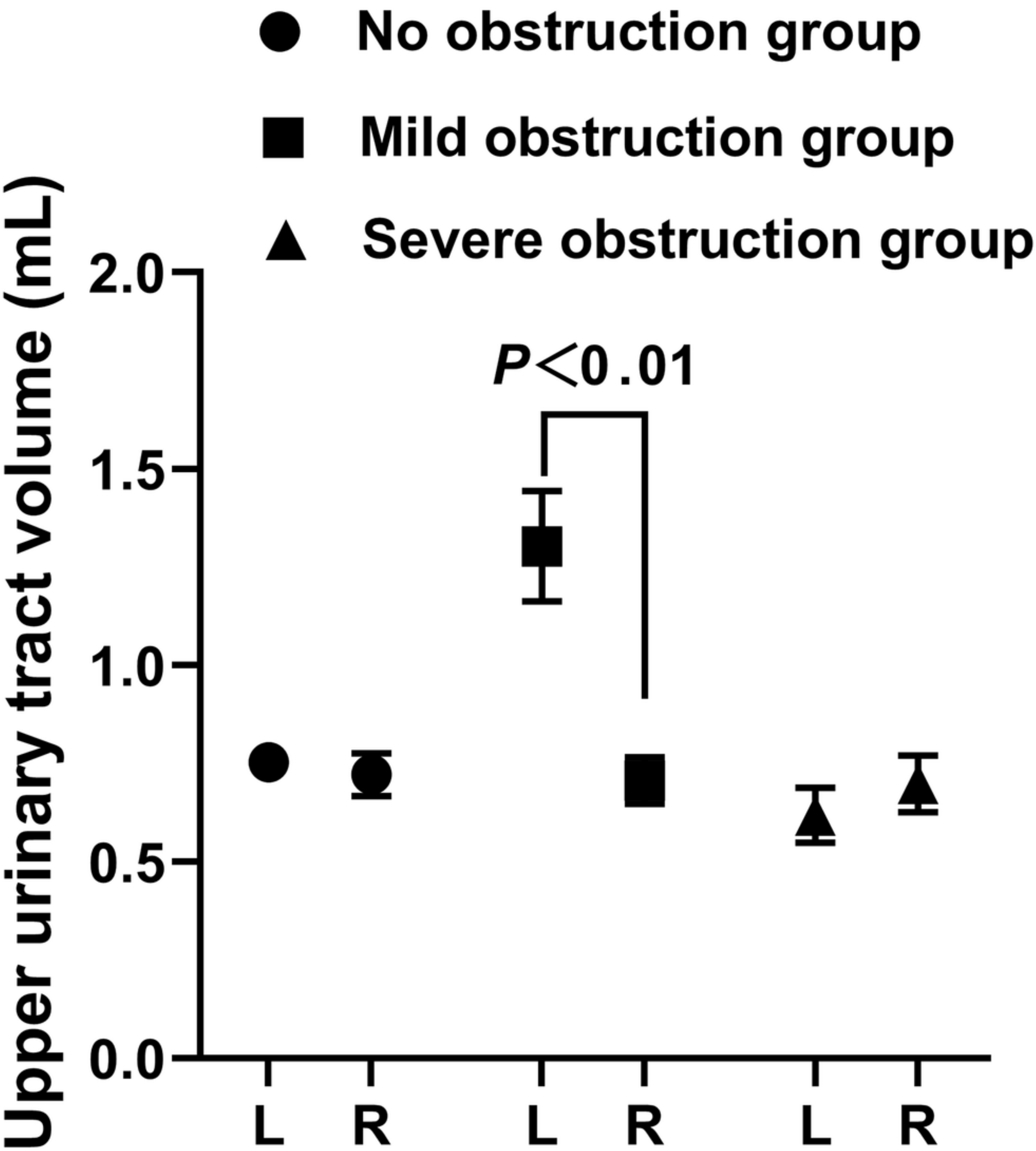


Figure 5

Comparison of extremum differences of upper urinary tract volume between different groups

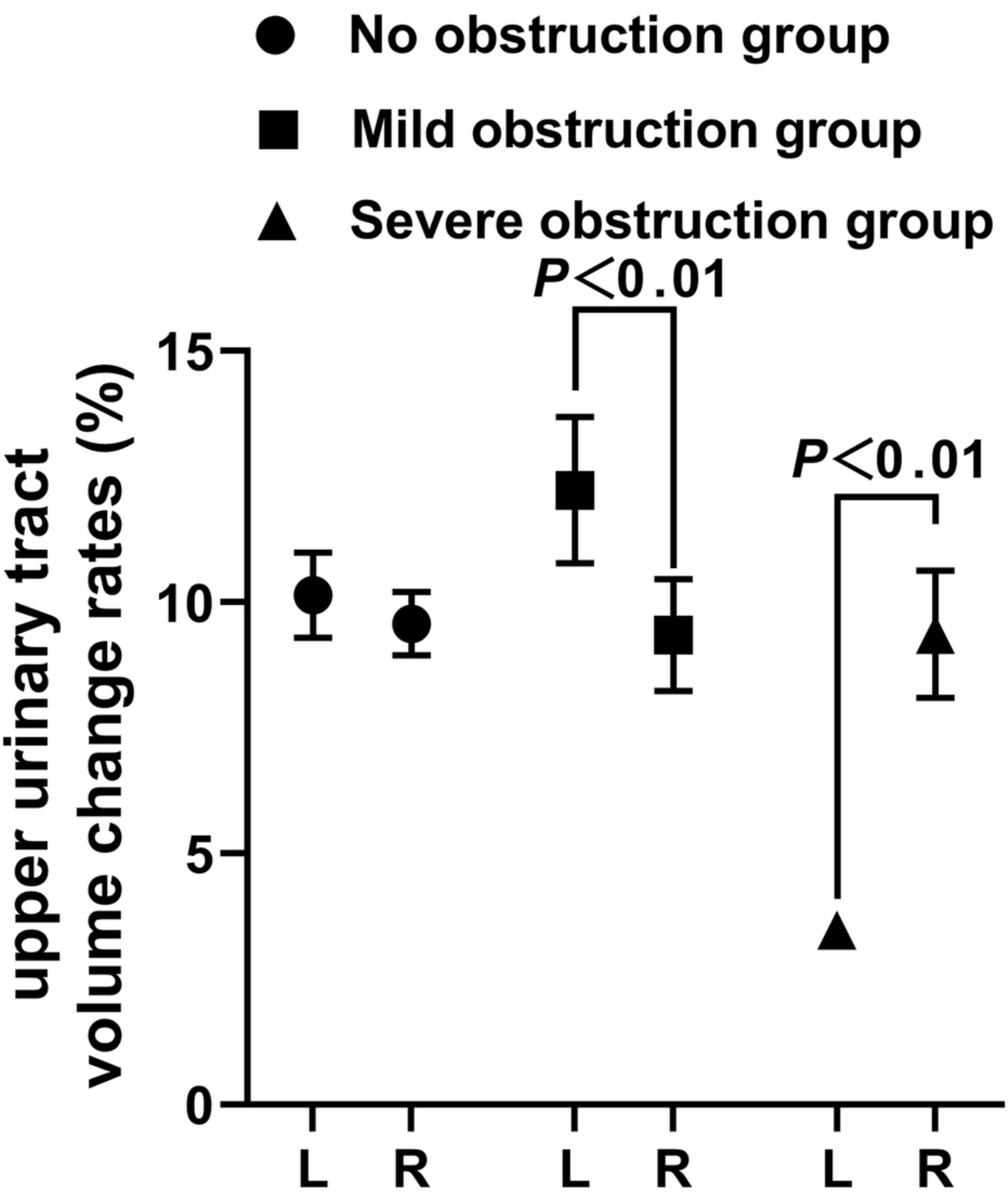


Figure 6

Comparison of upper urinary tract volume change rates among different groups

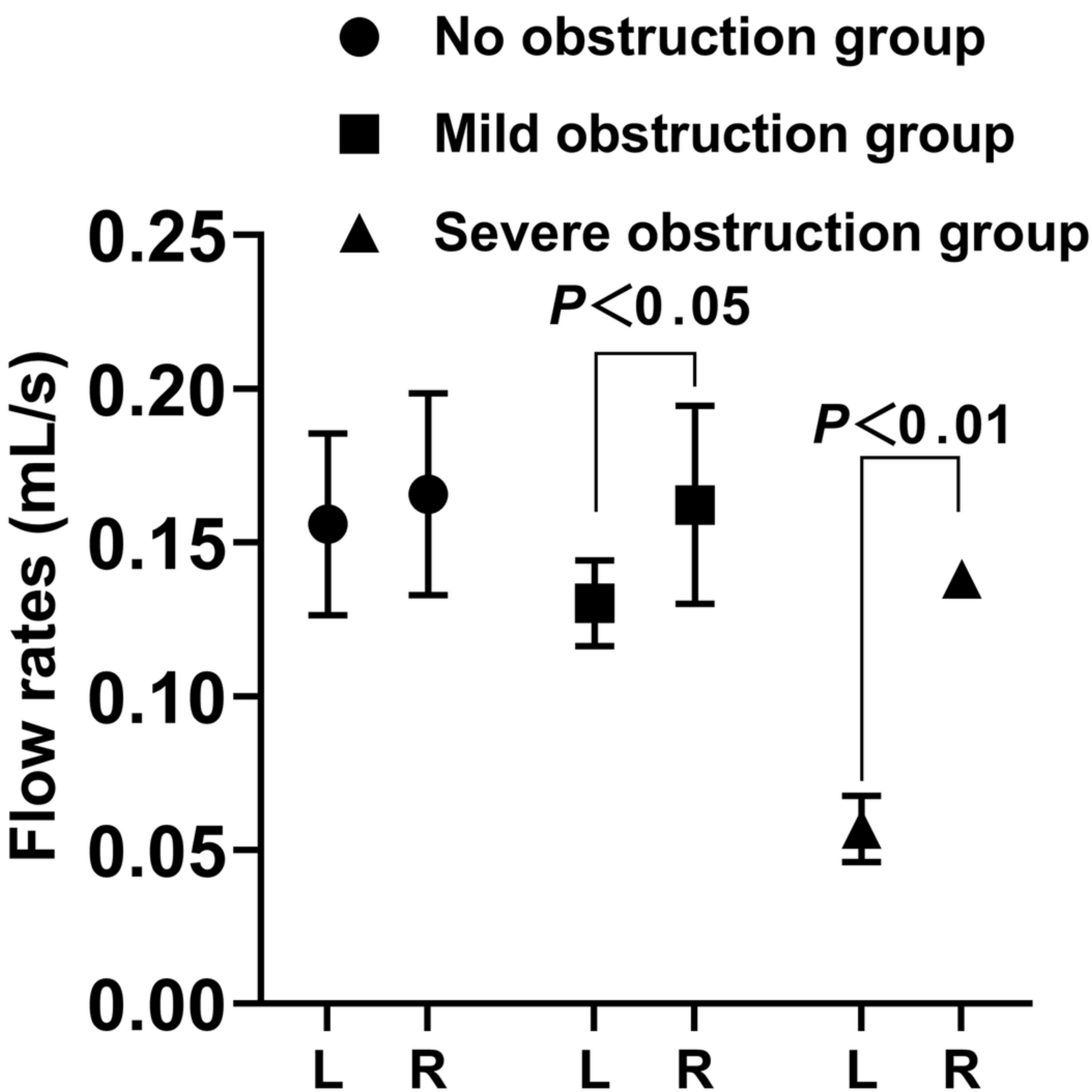


Figure 7

Comparison of calculated flow rates in the upper urinary tract between different groups

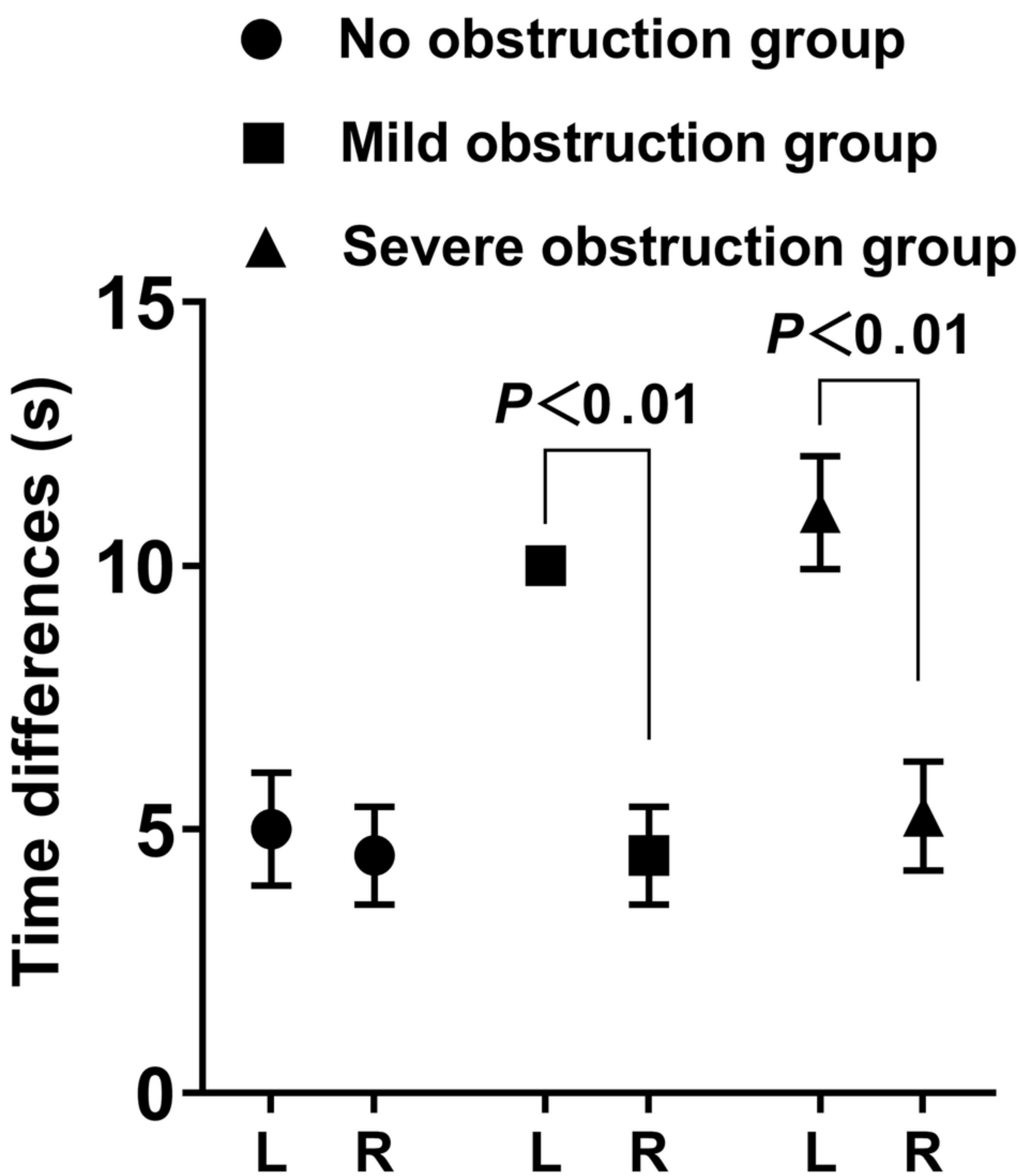


Figure 8

Comparison of time differences between extremum of upper urinary tract volume between different groups