Hypothesis / aims of study
Recently there have been some reports that tamsulosin is effective for discharge of ureter stones. The relation between voiding function of the lower urinary tract and alpha1-adrenoceptor (AR) is well known, and is applied clinically. On the other hand, there has been little research into alpha1-AR of the upper urinary tract. We studied the expression and role in ureteral contraction of alpha1-AR subtypes, which was considered to clarify the mechanism of ureteral urodynamics and passing ureter stones.

Study design, materials and methods
Specimens were taken from patients with renal cancer (n=12) or bladder cancer (n=13) who were not treated before surgery. Expression of alpha1-AR subtypes was examined by immunostain and Western blot, and each alpha1-AR subtype mRNA content was measured by quantitative RT-PCR. In the functional experiments, ureter was cut into longitudinal or spiral segments. One of these segments was suspended longitudinally in an organ bath containing Krebs solution gassed with a mixture of 95% oxygen and 5% carbon dioxide at 37°C. The tissue’s response was measured by means of an isometric force-transducer. Effects of silodosin (alpha1A-AR antagonist), tamsulosin (alpha1A/D-AR antagonist) and BMY-7378 (alpha1D-AR antagonist) were evaluated on phenylephrine (alpha1-AR agonist)-induced contraction, which was expressed as percentage of the maximal response.

Results
Alpha1A-AR and alpha1D-AR were detected by both immunohistochemistry and Western blot clearly. But alpha1B-AR was hardly detected. Alpha1-AR subtype mRNA content was measured by quantitative RT-PCR. In the functional experiments, ureter was cut into longitudinal or spiral segments. One of these segments was suspended longitudinally in an organ bath containing Krebs solution gassed with a mixture of 95% oxygen and 5% carbon dioxide at 37°C. The tissue’s response was measured by means of an isometric force-transducer. Effects of silodosin (alpha1A-AR antagonist), tamsulosin (alpha1A/D-AR antagonist) and BMY-7378 (alpha1D-AR antagonist) were evaluated on phenylephrine (alpha1-AR agonist)-induced contraction, which was expressed as percentage of the maximal response.

Interpretation of results
Alpha1A-AR mRNA expression is the highest among alpha1-AR subtypes in the human ureter. However, the alpha1A-AR which contributed most to contraction was alpha1A-AR.

Concluding message
This is the first study about the relation between alpha1-AR and human ureter contraction. In this study, the possibility that alpha1A-AR blocking agent was useful for discharge of ureter stones was suggested. Furthermore, it seems to be important for the research into ureteral peristalsis and drug development for ureteral contraction and relaxation.
Fig. 2  Antagonistic effect of tamsulosin in the isolated human ureter

Fig. 3  Antagonistic effect of BMY-7378 in the isolated human ureter

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HUMAN SUBJECTS:  This study was approved by the The ethics committee of Nagoya City University Graduate School of Medical Sciences and followed the Declaration of Helsinki. Informed consent was obtained from the patients.