



# Relationship of blood flow in the common iliac vein to lower urinary tract disease

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## Abstract

**Purpose** The relationship between blood flow and lower urinary tract disease was explored by measuring blood flow in the common iliac vein to examine the influence of pelvic congestion on lower urinary tract symptoms.

**Methods** Color Doppler ultrasonography of the right common iliac vein was performed in 113 men and 60 women, who were outpatients of two Japanese hospitals. Average blood flow velocity and cross-sectional area of the vein were measured, and blood flow volume was calculated. The relationship between these parameters and age or urological diseases was then examined.

**Results** There was no relation between age and average blood flow velocity or blood flow volume of the common iliac vein in either men or women. However, average common iliac vein blood flow velocity was significantly lower in men with chronic prostatitis and in women with overactive bladder than in other male and female patients, respectively. Common iliac vein blood flow volume was also significantly lower in men with chronic prostatitis than in other male patients.

**Conclusions** Men with chronic prostatitis and women with overactive bladder have low blood flow in the common iliac vein, suggesting that pelvic congestion may be related to these two conditions.

**Keywords** Prostatitis · Overactive bladder · Common iliac vein · Blood flow · Pelvic congestion

## Introduction

The association between metabolic syndrome and lower urinary tract symptoms (LUTS) has been attracting considerable attention [1–3]. Hypertension is one of the diseases associated with metabolic syndrome, and it may also be relevant to LUTS. Spontaneously hypertensive rats are reported to have a significantly reduced bladder capacity and

voiding volume [4]. These rats also have low blood flow in the prostate gland and prostatomegaly [5]. In a rat model of atherosclerosis-induced chronic bladder ischemia, voiding frequency was increased due to detrusor overactivity [6]. Atherosclerosis is associated with metabolic syndrome and is thought to be a risk factor for benign prostatic hyperplasia (BPH), with a relationship between high vascular resistance (a high resistive index on Doppler ultrasonography) and BPH being suggested [3, 5]. Therefore, it is possible that progression of hypertension and/or arteriosclerosis associated with metabolic syndrome leads to reduced arterial blood flow and ischemia, which induces BPH or overactive bladder (OAB).

Pelvic congestion syndrome is a chronic condition in women that is associated with varicose veins in the lower abdomen [7, 8]. The chief symptom is chronic pain, often described as a constant dull ache, which may be aggravated by standing. It has also been suggested that chronic prostatitis in men is related to pelvic congestion. Our previous study revealed that inferior vena cava (IVC) reflux was related to chronic prostatitis in men and to stress incontinence in

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women [9]. IVC reflux may originate from tricuspid regurgitation, which has a very high prevalence of 70% among adults in Japan [10] and 17–68% among persons with otherwise “normal” hearts in the USA [11, 12]. Accordingly, low oxygenation associated with pelvic venous congestion could promote lower urinary tract dysfunction, in addition to pelvic ischemia caused by hypertension and arteriosclerosis. However, there have been no reports about the relationship between pelvic venous blood flow and lower urinary tract disease or LUTS.

To examine the influence of pelvic congestion on LUTS, blood flow in the common iliac vein was measured in the present study, after which the relationship between blood flow parameters and lower urinary tract disease was explored.

## Patients and methods

Between January 2012 and December 2014, new adult patients visiting the outpatient clinics of Okinawa Kyodo Hospital and Kitakami Central Hospital in Japan underwent transabdominal ultrasonography of the urinary tract and color Doppler ultrasonography of the right common iliac vein. While measurement of blood flow in the internal iliac vein may provide a better indication of pelvic congestion, it is sometimes difficult to perform, so we measured blood flow in the right common iliac vein of the examiner’s side instead. A total of 113 men (aged 27–96 years) and 60 women (aged 27–93 years) in whom right common iliac vein blood flow could be successfully measured were enrolled in this study. The Okinawa Kyodo Hospital Ethics Committee approved the conduct of this study on behalf of the two participating institutions, and each patient provided informed consent for participation in the study prior to enrolment.

Among the 113 men, 63 had BPH, 17 had chronic prostatitis, and 11 had bladder cancer. BPH was diagnosed in men with LUTS and prostatomegaly (prostate volume > 20 ml). Chronic prostatitis was diagnosed in men with LUTS, including lower abdominal or perineal discomfort or pain, voiding pain, and urinary frequency or urgency, who had prostate tenderness on examination and no fever. Detailed classification of prostatitis [13] was not always performed. Among the 113 male patients, 37 had either OAB alone or in combination with BPH or chronic prostatitis. OAB was diagnosed in men who had LUTS, including urinary urgency and frequency or nocturia with or without urgency urinary incontinence, and without urinary tract infection or other obvious pathology, such as bladder stones or bladder cancer [14]. Among the 60 women, 25 had OAB, 11 had cystitis, and five had hematuria.

Transabdominal color Doppler ultrasonography of the right common iliac vein was performed by six ultrasound

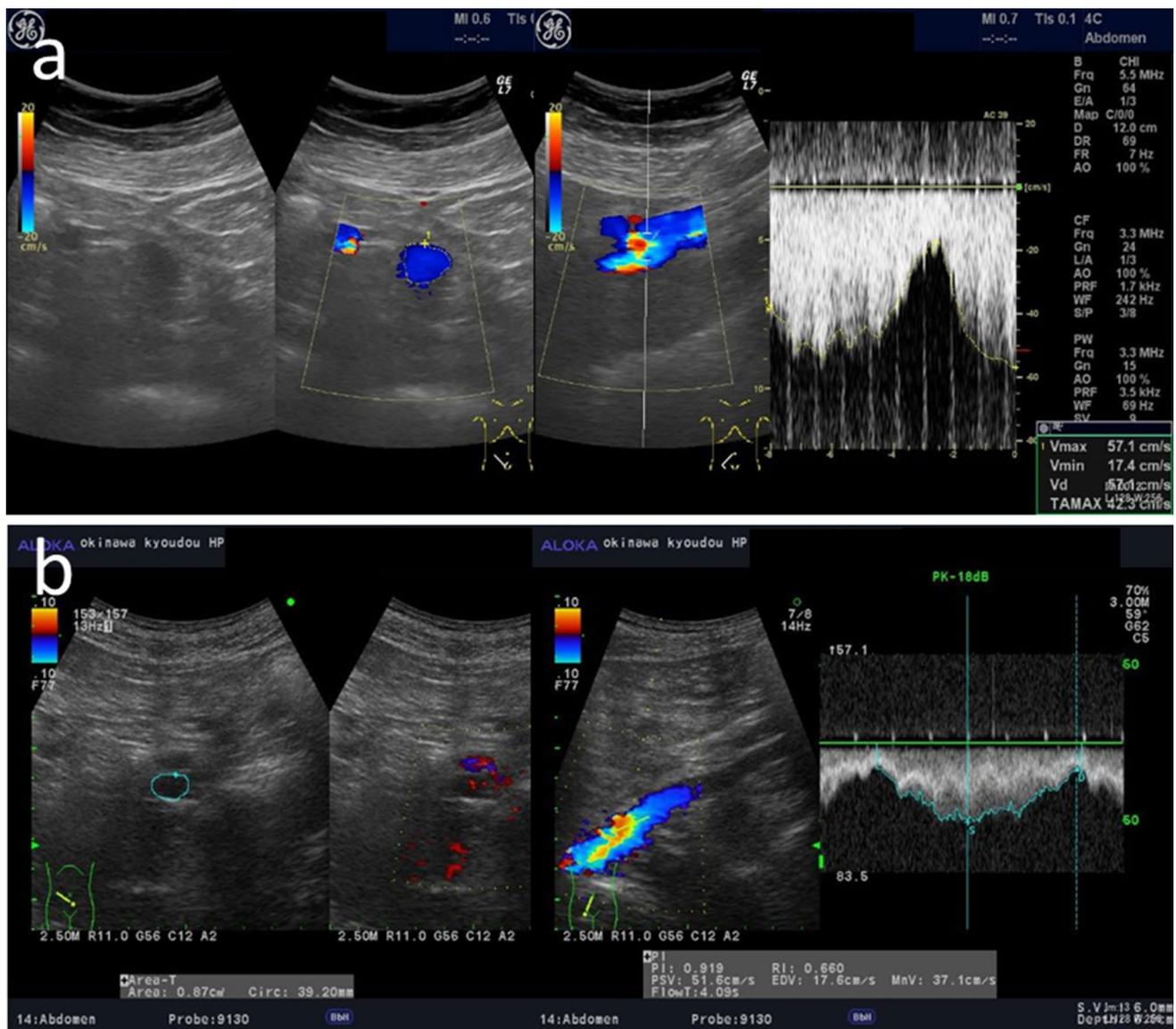
examiners and one urologist (KS) as follows. Blood flow velocity was measured using a LOGIQ7 with a convex 4C probe (2.0–5.5 MHz) (GE Healthcare Japan, Tokyo, Japan), a ProSound SSD- $\alpha$ 10 with a UST-9130 convex probe (2.5 MHz) (Aloka, Tokyo, Japan), and an SSA-590A with a convex probe (3.75 MHz) (Toshiba Medical Systems, Tokyo, Japan). With the patient in the supine position, the convex probe was placed diagonally on the right lower abdominal wall, and the velocity was set at 13 cm/s for color Doppler studies. The average blood flow velocity and cross-sectional area were then measured at the midpoint of the right common iliac vein (Fig. 1), and the blood flow volume was calculated. Blood flow in the right common iliac vein could be measured in all patients with informed consent. The relationship between right common iliac vein blood flow parameters (average blood flow velocity, cross-sectional area, and blood flow volume) and age or urological disease was examined on the basis of the final diagnosis made for each patient. In male patients, the relationship between age and prostate volume ( $4\pi/3 \times \text{length}/2 \times \text{width}/2 \times \text{height}/2/1/2 \times \text{length} \times \text{width} \times \text{height}$ ) measured by transabdominal ultrasonography was also examined.

Results are reported as the mean  $\pm$  standard deviation. Student’s *t* test was used for statistical analysis and  $p < 0.05$  was considered to indicate statistical significance.

## Results

In the 113 male patients, there was a significant positive correlation between age and prostate volume ( $p < 0.001$ ), but no relation of age to average blood flow velocity, cross-sectional area, or blood flow volume of the right common iliac vein (Fig. 2). When male patients with BPH or bladder cancer were compared to the other male patients, there were also no significant differences in average blood flow velocity, cross-sectional area, or blood flow volume. However, when 17 patients with chronic prostatitis (aged 27–79 years) and 71 other age-matched male patients (aged 27–79 years) were compared, there were significant differences in prostate volume ( $20.0 \pm 8.9$  vs.  $30.7 \pm 18.1$  ml,  $p = 0.017$ ), average blood flow velocity in the right common iliac vein ( $23.0 \pm 10.7$  vs.  $33.0 \pm 16.8$  cm/s,  $p = 0.018$ ), and blood flow volume of the common iliac vein ( $24.1 \pm 9.9$  vs.  $37.1 \pm 24.1$  ml/s,  $p = 0.026$ ) (Fig. 3). In the male group, 37 patients had OAB. When male patients with or without OAB were compared, there were no significant differences in average blood flow velocity, cross-sectional area, or blood flow volume of the right common iliac vein.

In the 60 female patients, a significant positive correlation was identified between age and cross-sectional area of the right common iliac vein ( $p = 0.049$ ), but not between age and average blood flow velocity or blood flow volume of the



**Fig. 1** Measurement of the diameter of the right common iliac vein and blood flow velocity in the vein (2 patients). **a** Patient with high blood flow velocity. **b** Patient with low blood flow velocity. For both

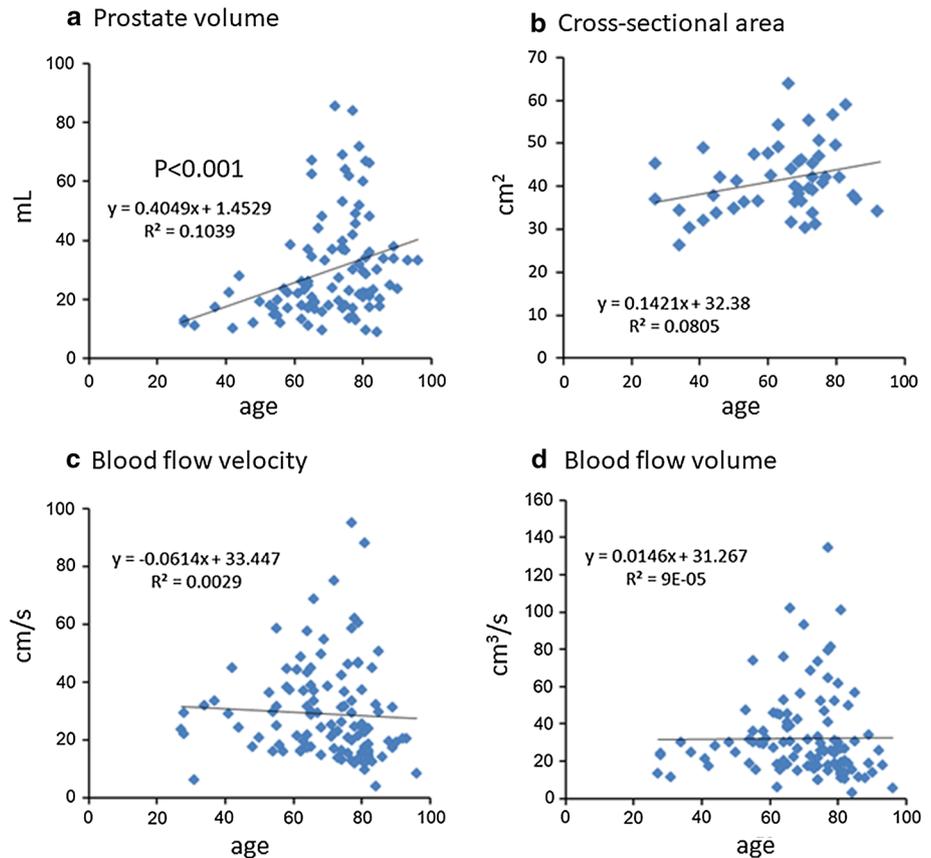
patients, the left figures show measurement of the cross-sectional area of the right common iliac vein and the right figures show measurement of the blood flow velocity

vein (Fig. 4). The female group included 25 patients with OAB (aged  $66.1 \pm 13.5$  years) and 35 patients without OAB (aged  $61.4 \pm 18.2$  years), and there was a significant difference in average blood flow velocity in the right common iliac vein between them ( $26.8 \pm 11.3$  vs.  $34.9 \pm 19.9$  cm/s, respectively,  $p=0.041$ ) (Fig. 5). However, there was no significant difference in blood flow volume in the common iliac vein between female patients with OAB and without OAB ( $28.8 \pm 17.2$  ml/s vs.  $39.0 \pm 30.5$  ml/s). When female patients with and without cystitis were compared, no significant differences were observed with regard to average blood flow velocity, cross-sectional area, or blood flow volume of the right common iliac vein.

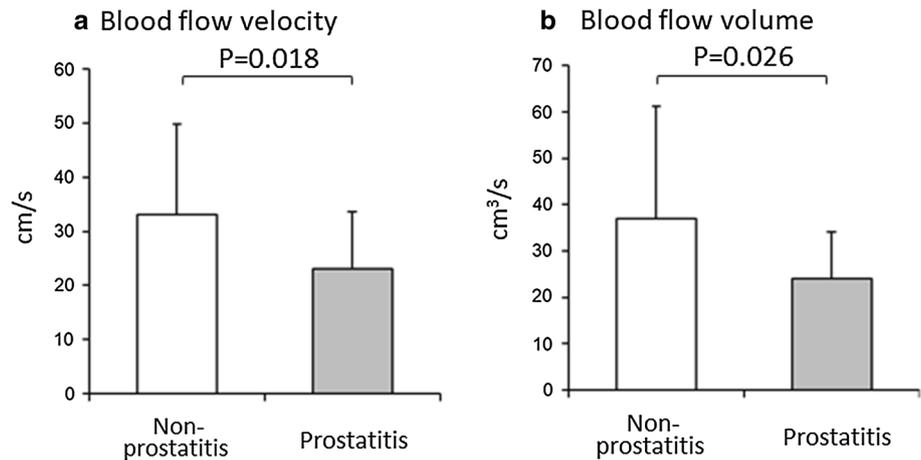
## Discussion

In the present study, a significant positive correlation was observed between age and cross-sectional area of the right common iliac vein in female patients, but there were no correlations between age and average blood flow velocity or blood flow volume of the right common iliac vein in either male or female patients. However, in male patients with chronic prostatitis and female patients with OAB, average blood flow velocity in the right common iliac vein was significantly lower than in the other male and female patients, respectively. In addition, blood flow volume in the right common iliac vein was significantly lower in male patients

**Fig. 2** Relationship between age or prostate size and cross-sectional area, blood flow velocity, or blood flow volume of the right common iliac vein in men. In 113 male patients, there was a significant positive correlation between age and prostate volume, but not between age and average blood flow velocity, cross-sectional area, or blood flow volume of the right common iliac vein



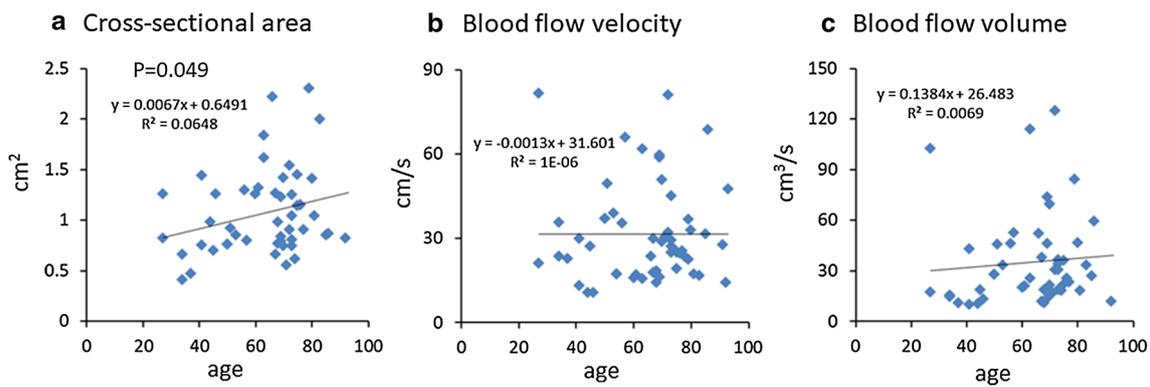
**Fig. 3** Comparison of blood flow velocity and blood flow volume of the right common iliac vein between men with or without chronic prostatitis. When the 17 patients with chronic prostatitis (aged 27–79 years) were compared to 71 age-matched male patients without prostatitis (aged 27–79 years), there were significant differences in average blood flow velocity ( $23.0 \pm 10.7$  vs.  $33.0 \pm 16.8$  cm/s, and  $p = 0.018$ ) and blood flow volume ( $24.1 \pm 9.9$  vs.  $37.1 \pm 24.1$  ml/s, and  $p = 0.026$ )



with chronic prostatitis than in the other male patients. Thus, men with chronic prostatitis and women with OAB displayed low blood flow in the common iliac vein, suggesting that pelvic congestion may be one of the factors contributing to these conditions.

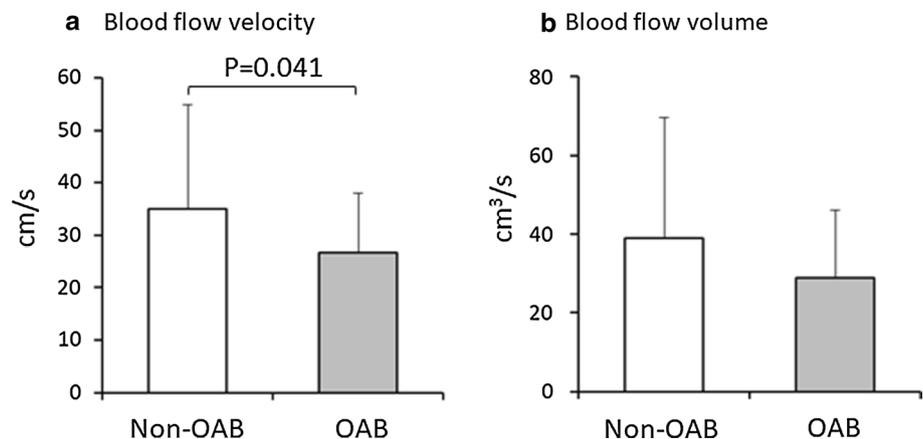
It has been proposed that pelvic congestion is responsible for the pathology underlying chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) [9, 15]. Regarding the association between reflux of blood into the inferior vena

cava due to tricuspid regurgitation and urological diseases, a significant increase in inferior vena cava reflux has been reported in men with chronic prostatitis [9], suggesting that pelvic congestion secondary to inferior vena cava reflux might contribute to the development of refractory prostatitis with or without overt symptoms. In addition, it has been reported that many patients with prostatitis also have hemorrhoids, which may be attributable to pelvic congestion [15]. Prolonged walking and sitting lead to exacerbation of the



**Fig. 4** Relationship between age and cross-sectional area, blood flow velocity, or blood flow volume of the right common iliac vein in women. In the 60 female patients, there was a significant positive correlation between age and cross-sectional area of the right common iliac vein ( $p=0.049$ ), but not between age and average blood flow velocity or blood flow volume

**Fig. 5** Comparison of blood flow velocity and blood flow volume of the right common iliac vein between women with or without OAB. When the 25 female patients with OAB (aged  $66.1 \pm 13.5$  years) were compared to the 35 female patients without OAB (aged  $61.4 \pm 18.2$  years), there was a significant difference in average blood flow velocity ( $26.8 \pm 11.3$  vs.  $34.9 \pm 19.9$  cm/s, and  $p=0.041$ )



symptoms of CP/CPPS, while lying down alleviates these symptoms, which also suggests a role of pelvic congestion [9]. The pathogenesis of CP/CPPS is probably multifactorial, and the main condition causing symptoms is likely to differ among patients, but it seems important to consider pelvic circulatory disturbance as a possible factor.

Carbazochrome sodium sulfonate (carbazochrome) is a stable oxyepinephrine derivative that acts as a capillary stabilizer and is used to treat hemorrhage due to capillary fragility [16]. Although its mechanism of action is still unclear, the recent studies have suggested that it reverses the increase in endothelial cell permeability induced by thrombin, trypsin, and bradykinin via the inhibition of intracellular actin stress fiber formation and restoration of intercellular tight junctions [17, 18]. These reports suggest that treatment with carbazochrome may reduce extravascular leakage of blood. In a recent clinical study, we found marked improvement of pain when patients with refractory chronic prostatitis were treated with carbazochrome, as well as improvement of storage symptoms and post-micturition symptoms [19]. Because carbazochrome has not

been reported to have a diuretic effect or anti-inflammatory activity [17], its above-mentioned actions may be related to reduction of capillary permeability. Based on these results and our present findings, it is suggested that chronic prostatitis could be induced by extravascular leakage of blood due to pelvic venous congestion.

In our female patients with OAB, the average blood flow velocity was also low in the right common iliac vein, suggesting that extravascular leakage of blood due to pelvic venous congestion might contribute to OAB as well as to chronic prostatitis. In rats with tranilast-induced interstitial cystitis and increased vascular permeability in the bladder, the interval between bladder contractions is shortened and locomotor activity is reduced [20]. Administration of carbazochrome to these rats decreases bladder vascular permeability, prolongs the interval between bladder contractions, and improves locomotor activity, suggesting that carbazochrome treatment may inhibit the extravascular leakage of a bladder-stimulating factor [20]. Therefore, it is possible that an increase in vascular permeability due to pelvic congestion and consequent extravascular leakage of this

putative bladder-stimulating factor contribute to occurrence of LUTS, including OAB. However, there was no significant difference in the average blood flow velocity or blood flow volume of the right common iliac vein between our male patients with or without OAB. A possible explanation for this finding is that BPH was the most common diagnosis among men in this study population, and BPH itself causes OAB with or without pelvic congestion.

The prevalence of tricuspid regurgitation is very high and has been reported to be 70% among adults in Japan [10] and 17–68% among persons with otherwise “normal” hearts in USA [11, 12]. Therefore, it is difficult to conclude that inferior vena cava reflux due to tricuspid regurgitation generally causes pelvic congestion and induces lower urinary tract symptoms. However, we have previously reported a woman with pelvic congestion who had inferior vena cava reflux due to tricuspid regurgitation and no valves in the pelvic venous system on venography [21]. This suggests that inadequate valves in the pelvic veins could be related to pelvic congestion, and poor venous valves may also be related to tricuspid regurgitation [22]. Regardless of the cause, pelvic congestion could be one of the factors contributing to the occurrence of LUTS.

## Conclusion

Men with chronic prostatitis and women with overactive bladder have low blood flow in the common iliac vein, suggesting that pelvic congestion may be involved in the etiology of these conditions. However, there are some limitations in this study. First, this is a study conducted at two institutions and performed by several examiners. Thus, differences in accuracy between the institutions or examiners should be evaluated. Second, we examined blood flow only in the right common iliac vein. Common iliac vein data are affected by the flow status of the external iliac vein as well as the internal iliac vein. Thus, patients with femoral artery and lower limb peripheral artery atherosclerosis, which causes lower flow of the external iliac vein, should have been excluded. It is better to measure and compare the blood flow in the internal iliac arteries and veins on both sides. In the future, we would like to investigate blood flow measurement of the internal iliac arteries and veins.

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## Compliance with ethical standards

**Conflict of interest** The authors have no conflicts of interest to declare.

**Ethical statement** This study was approved by the Medical Ethics Committee of Okinawa Kyodo Hospital on behalf of the two participating facilities, and informed consent was obtained from all patients enrolled in the study.

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