The Role of Intraabdominal Pressure in Venous Blood Drainage from the Prostate into the Vertebral Vein System

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Abstract We investigated venous blood drainage from the prostate into the vertebral vein system by cineangiography in five mongrel dogs and measured intraabdominal pressure and venous blood pressure in the dog or human to study the role of intraabdominal pressure in the drainage. The averages of intraabdominal pressure and caudal vena caval pressure in the dog were 32.2±3.0 and 12.8±1.3 mmHg, respectively, in the supine position, and 39.2±3.0 and 23.8±4.0 mmHg, respectively, in the head-up tilt position, when the radiopaque medium injected into the dorsal penile vein appeared in the vertebral vein system. Intraabdominal pressure in the head-up tilt position was significantly higher than that in the supine position when the venous drainage into the vertebral veins happened. In eight continuous ambulatory peritoneal dialysis patients, intraabdominal pressure showed 8.1±2.4 mmHg in the supine position, 24.6±4.3 mmHg in the sitting position, and 30.4±4.9 mmHg in the standing position at rest. During voluntary contraction of the abdominal muscles, the pressure was increased up to 50.6±21.6 mmHg in the supine position, 69.3±19.8 mmHg in the sitting position, and 73.8±19.8 mmHg in the standing position. These pressure values in the human were significantly higher than those observed at the time when the radiopaque medium appeared in the vertebral veins in both supine and head-up tilt positions in the canine. These results suggest that the increase of intraabdominal pressure causes inflow of prostatic venous blood into the vertebral veins via the inferior vena cava, common iliac vein, or internal iliac vein.

Key words: vertebral vein system, prostate, intraabdominal pressure.

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The prostatic vein is well known to indirectly connect with the vertebral veins. Batson [1, 2] observed that the contrast medium injected in the deep dorsal vein of the penis spread into the vertebral veins in human cadavers. Clinically, prostate cancer metastasizes preferentially to bones, especially the pelvis, sacrum, and lumbar spine [3–5], and the above pathway has supposed to be related to metastasis of the prostate cancer to the vertebral column. Batson [1] also showed the same phenomenon in living rhesus monkeys when their abdomina were compressed as he observed in human cadavers. From these observations, he hypothesized that cells of prostate cancer may spread to the vertebral column via the vertebral vein system which bypasses the inferior vena cava. It has been also demonstrated by other researchers that this route contributes to metastases of prostate cancer to the vertebral column [6–8]. Therefore, the dynamic analysis of the blood flow from the prostate into the vertebral vein system is clinically as well as physiologically very important.

The mechanism of inflow of the prostatic venous blood into the vertebral vein system is thought to be related to not only their anatomical connection but also the elevation of intraabdominal pressure. The urinary bladder outlet with a swollen prostate gland is variously obstructed, and the patients with the outlet obstruction often use a Valsalva maneuver during urinary flow so as to obtain a high intravesical pressure [9]. Kurokawa et al. [10] and Suzuki et al. [11] observed by cineangioigraphy with a fluoroscope that venous blood from the prostate gland flows into the vertebral vein system in dogs when intraabdominal pressure is elevated. However, their studies were performed only in the supine position, and the pressure of the abdominal cavity and the caudal vena cava under different postures has not been measured. To study the role of intraabdominal pressure in venous blood drainage from the prostate into the vertebral vein system more in detail, we investigated pressure changes in the caudal vena cava and the abdominal cavity in relation to the venous drainage of the prostate into the vertebral vein system in dogs, and changes in intraabdominal pressure under different postures as well as during voluntary contractions of abdominal muscles in humans.

MATERIALS AND METHODS

Animal experiments. Five dogs, weighing 9–13 kg, were anesthetized with pentobarbital sodium (30 mg/kg, Abbott Laboratories, Illinois) injected intramuscularly. After administration of atropine sulfate (0.2 mg/canine), pancuronium bromide was injected intravenously to avoid muscle movements. The animals were ventilated with room air by an artificial respirator (Shinano Co., Tokyo, Japan) to prevent suppression of respiratory movement which would be produced by an increase of the intrathoracic pressure during abdominal compression. All experiments were carried out at the Institute of Experimental Animal Research in Gunma University School of Medicine, and all animals were treated according to the “Guide for the Care and Use of Laboratory Animals” of this Institute.
ABDOMINAL PRESSURE AND VENOUS DRAINAGE OF THE PROSTATE

To detect the pathways of the venous flow into the vertebral vein system from the prostatic tissues, first the penis was incised on the dorsal side and a catheter was inserted into the dorsal vein of the penis. After that, 0.5−1.0 ml of lipiodol Ultra-Fluide (Laboratoire Guerbet, France) was injected into the dorsal vein of the penis for 30 s at a bolus, and the stream of the radiopaque medium was continuously observed by cineangiography with a fluoroscope (65 kV, 37 mA·s) (XED150L-10A Shimadzu Corporation, Kyoto, Japan). The observation was performed in both the supine and 90° head-up tilt position. The results were recorded on videotapes (VC-30 Sharp, Tokyo, Japan) and the radiographs were printed from the videotapes for later analysis.

To measure venous blood pressure and intraabdominal pressure, two catheters were used. One was introduced into the right femoral vein, and the tip of the catheter was placed at the level of the external iliac vein to measure its blood pressure. To detect pressure in the common iliac vein and the caudal vena cava, the catheter was pushed toward the heart and it was confirmed by fluoroscopy that the tip of catheter was placed in the proper portion. The other was inserted into Douglas’s cavity at the midline of the abdominal wall. The position of the tip of catheter was identified also by fluoroscopy. After 1,000 ml of physiological saline was infused into the abdominal cavity through the catheter, the catheter was connected with a pressure transducer. The abdomen was bound with a towel at the level of the second lumbar vertebra, which was used later to increase intraabdominal pressure. The pressure of the intraabdominal cavity and the caudal vena cava was simultaneously measured with transducers (type 45265, NEC San- ei Instrument Ltd., Tokyo, Japan). Venous pressure was electrically averaged with a time constant of 3 s. Intraabdominal pressure at rest was calculated as an average value in the recorded pressure profile with a time constant of 3 s. The right atrium was defined as the physiological reference point (0 mmHg) of these pressure measurements.

Measurements of intraabdominal pressure in the human. Intraabdominal pressure was measured in eight patients aged 17 to 76 years (average age: 46 years) who suffered from the chronic renal failure and underwent continuous ambulatory peritoneal dialysis (CAPD). Six of these patients suffered from chronic glomerular nephritis, one from polycystic kidney, and one from diabetic nephropathy. A catheter was inserted into the abdominal cavity of each patient to infuse dialytic solution. Intraabdominal pressure was measured through this catheter. The right atrium was defined as the physiological reference point (0 mmHg) of the intraabdominal pressure measurements same as the animal study. Two thousand ml of dialytic solution was infused into the abdominal cavity in six patients and 1,500 ml in the two other patients. The pressure in each patient was measured in three different positions: supine, sitting, and standing, and the pressure was measured both in a relaxed state and during voluntary contraction of the abdominal muscles in each position.

The patients were informed that this experimental procedure is entirely safe
and painless during and after the measurement of intraabdominal pressure, and that the experimental data from this experiment are very important to clarify the role of vertebral vein system in the vertebral column metastases of the prostatic cancer. All patients gave their consent.

Statistical analysis was carried out by using $F$ test and Student $t$-test. Significant differences were considered when $p$ value was less than 0.05.

RESULTS

Animal experiments

Fluoroscopic observations. During rest in the supine or head-up tilt position, the contrast medium flowed from the dorsal vein of the penis in two directions, but did not enter the vertebral vein system (Fig. 1a). In one route, the radiopaque medium entered the external iliac vein, flowed into both common iliac veins, and finally into the caudal vena cava. In the other route, the contrast medium first entered the internal pudendal vein, flowed into the internal iliac vein, into both common iliac veins, and finally into the caudal vena cava.

When the abdomen was tied and squeezed with a towel to increase intraabdominal pressure, the medium entered the vertebral vein system (Fig. 1b),

![Fig. 1. Venous angiograms taken following injection of the radiopaque medium into the dorsal penile vein (A). a: A venous angiogram taken in a right recumbent position. The contrast medium did not flow into the vertebral veins at rest or below 20 mmHg of intraabdominal pressure. In this case, the pressure was 20 mmHg. b: A venous angiogram taken in the supine position under 40 mmHg of intraabdominal pressure. The contrast medium entered the vertebral veins (arrows) from the caudal vena cava (B) and the common iliac (medial sacral) vein (C).](image)

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either in the supine or head-up tilt position. In the supine position, when the abdomen was lightly squeezed, that is, when increase of intraabdominal pressure was relatively small (about 30 mmHg), the contrast medium entered the vertebral vein system mainly through the caudal vena cava and lumbar veins at the portion of cranial lumbar vertebra; however, when it was strongly squeezed, that is, increase of intraabdominal pressure was relatively large (about 40 mmHg), the contrast medium flowed into the vertebral vein system via the internal iliac, common iliac veins, or the caudal portion of the caudal vena cava (Fig. 1b). In the head-up tilt position, when increase of intraabdominal pressure was relatively small (about 25 mmHg), the flow of the vena cava was observed to slow down or stop, and when the pressure of the abdominal cavity was markedly elevated (about 40 mmHg) the contrast medium appeared in the vertebral vein system at the portions of both cranial and caudal lumbar vertebrae.

*Intraabdominal pressure and venous pressure.* During rest, intraabdominal pressure was $7.3 \pm 0.4$ mmHg, and mean venous blood pressure was $5.8 \pm 1.0$ mmHg in the external iliac vein, $3.3 \pm 0.5$ mmHg in the common iliac vein, and $2.5 \pm 1.4$ mmHg in the caudal vena cava in the supine position. When the animals were tilted to the head-up position at right angles, intraabdominal pressure showed $15.8 \pm 0.7$ mmHg, and venous blood pressure showed $18.5 \pm 0.5$ mmHg in the external iliac vein, $17.0 \pm 0.3$ mmHg in the common iliac vein, and $14.0 \pm 0.1$ mmHg in the caudal vein.

![Fig. 2. Venous blood pressure of the right external iliac vein (EIV), the right common iliac vein (CIV), and the caudal vena cava (CVC) of the canine in the supine and head-up tilt position at rest. Venous pressure value of EIV in the supine position was significantly higher than those of CIV and CVC ($p < 0.05$), and the pressure of CVC in the head-up tilt position was significantly lower than those of EIV and CIV ($p < 0.05$). $n = 5$, $*p < 0.05$, $**p < 0.01$.](image)
vena cava (Fig. 2). Venous pressures in the head-up position at the three different portions were significantly higher than those observed in the supine position. Intraabdominal pressure and caudal vena caval pressure synchronously oscillated in accordance with the respiratory movements during rest in both positions, and the wave heights of intraabdominal pressure oscillation and the caudal vena caval pressure oscillation were 2 to 4 mmHg and 1 to 2 mmHg, respectively.

During the abdominal compression, pressures in the abdominal cavity and the veins increased (Fig. 3). Intraabdominal pressure and blood pressure in the caudal vena cava at the time when the contrast medium entered the vertebral vein system, were $32.2 \pm 3.0$ and $12.8 \pm 1.3$ mmHg, respectively, in the supine position (Figs. 4, 5), and were $39.2 \pm 3.0$ and $23.8 \pm 4.0$ mmHg, respectively, in the head-up tilt position (Figs. 4, 6). The caudal vena caval pressure in the head-up tilt position at the time when the venous drainage into the vertebral vein system began was higher than that seen in the supine position ($p < 0.05$). Intraabdominal pressure in the head-up tilt position when the drainage happened was also significantly higher than that in the supine position ($p < 0.01$).

**Intraabdominal pressure in humans**

At rest, intraabdominal pressure in CAPD patients was $8.1 \pm 2.4$ mmHg in the supine position, $24.6 \pm 4.3$ mmHg in the sitting position, and $30.4 \pm 4.9$ mmHg in the

![ECG](image1)

![IAP](image2)

![CVCP](image3)

**Fig. 3.** A typical record of intraabdominal (IAP) and caudal vena caval (CVCP) pressures with an abdominal compression maneuver in a dog. IAP and CVCP showed periodic changes under periodic abdominal compression, and both changes occurred synchronously.
Fig. 4. Average changes of intraabdominal pressure (IA) and caudal vena cava pressure (CVC) at the time when the contrast medium entered the vertebral vein system in the supine and head-up tilt positions. The pressure of IA was significantly higher than that of CVC in both supine and head-up tilt positions ($p < 0.05$). $n = 5$, *$p < 0.05$, **$p < 0.01$.

standing position. The value of intraabdominal pressure in the standing position was significantly higher than that in the both supine and sitting positions. When the patients contracted abdominal muscle with the maximum efforts, intraabdominal pressure extremely increased and reached $50.6 \pm 21.6$ mmHg in the supine position, $69.3 \pm 19.8$ mmHg in the sitting position, and $73.8 \pm 19.8$ mmHg in the standing position (Fig. 7). The value of intraabdominal pressure in the standing position during abdominal muscle contraction was significantly higher than that in the supine position, and also intraabdominal pressures during abdominal muscle contraction in three different postures were significantly higher than those at rest. Intraabdominal pressure during abdominal muscle contraction in patients with CAPD was significantly higher than that observed when the venous drainage into the vertebral vein system happened, both in the supine and head-up tilt positions in dogs.

DISCUSSION

Evidences of venous drainage of prostatic vein into the vertebral vein system. Venous blood from the prostate gland in the human usually drains into the prostatic vein, and follows the internal iliac vein, common iliac vein, and inferior vena cava to the right atrium. In anatomical textbooks, it has been described that the internal
Fig. 5. A record of changes in intraabdominal pressure (IAP) and caudal vena caval pressure (CVCP) when abdominal pressure was continuously elevated in the supine position in a dog. The contrast medium first appeared in the vertebral vein at about 30 mmHg of intraabdominal pressure (arrow). When IAP was increased very high, the contrast medium flowed more into the vertebral veins (double arrows).

iliac vein, common iliac vein, and inferior or caudal vena cava anastomose with the vertebral vein system through the lumbar and intervertebral veins in the dog and human [12, 13]. The vertebral vein system is valveless so that venous blood flow may be temporarily reversed by raising intraabdominal pressure [13]. Batson [1, 2] first noted that venous blood is squeezed out of the thoraco-abdominal cavity rather than being allowed to enter the cavity when strain or cough occurs. This phenomenon also applies to lift actions. In the same reports, he indicated, by injecting a contrast medium into the dorsal penile vein with abdominal compression, that the venous drainage into the vertebral vein system exists in living rhesus monkeys. In the present study we used cineangiography and confirmed that the venous drainage of the prostate flows into the vertebral vein system in the dog when pressure of the abdominal cavity is elevated.

The existence of the pathway above described has been clinically suggested since Batson [2] suggested that prostate cancer may spread out to vertebral column via the vertebral vein system without clinical findings of lung metastases. Franks [14] showed the existence of this route in human cadavers by injecting a barium suspension into the penile vein and by observing with X-ray radiography, and also found some barium deposits in the vertebral bony tissues by histological survey. On
Fig. 6. A record of changes in intraabdominal pressure (IAP) and caudal vena caval pressure (CVCP) with continuous abdominal compression in the head-up tilt position when the contrast medium entered the vertebral veins (arrow). When IAP was slightly elevated from the pressure at which the first entrance of contrast medium into the vertebral veins was observed, CVCP increased markedly and the contrast medium flowed more into the vertebral veins (double arrows).

dog cadavers, Leav and Ling [15] showed the similar findings that the contrast medium injected into the internal iliac vein appears in the vertebral column. It has been reported that skeletal metastasis is developed via the tail vein of rats and mice after inoculating tumor cells in the tail vein if abdominal compression or temporal occlusion of the inferior vena cava was concurrently performed [6–8].

The pathway of this venous drainage into the vertebral vein system plays a physiological role as a bypass of the inferior vena cava. It is also important in the metastasis mechanism of prostate cancer, because malignant cells spread to the vertebral column via the vertebral vein system and its inflow phenomenon is thought to strongly relate with the elevation of intraabdominal pressure as described above. However, the role of intraabdominal pressure in the venous drainage into the vertebral vein system has not been quantitatively clarified.

The value of intraabdominal pressure to produce venous drainage from the prostatic vein into the vertebral vein system. In the present study, the vena caval blood of the canine flowed into the vertebral veins when the intraabdominal
pressure increased, and the pressure value at the time when venous blood of abdominal vena cava began to enter the vertebral vein system was 32.2 ± 3.0 mmHg. Dopman et al. [16] reported that the infradiaphragmatic vena caval segment was narrowed and collapsed when the intraabdominal pressure increased to 10 to 40 mmHg in the presence of intraabdominal fluid, and the vena caval blood flowed into the vertebral vein system in the supine position in the canine. They also observed the presence of infradiaphragmatic vena caval constriction in a young female with massive ascites, whose intraabdominal pressure was less than 40 mmHg. The cross area of the inferior vena caval outlet from the abdomen decreases by 80% during a deep inspiration, and the pressure gradient between the abdominal cavity and the thoracic cavity detected at the level of the orifice of the diaphragm shows 20 mmHg [17]. Therefore, in the supine position, if intraabdominal pressure is elevated up to about 30 mmHg as shown in our study, the vena cava will be collapsed at the caudal side of the diaphragm, and the blood of the vena cava may flow into the vertebral veins because blood pressure of the peripheral veins will increase. CAPD patients were able to increase easily the intraabdominal pressure over 32 mmHg by contracting the abdominal muscles in the supine position. It is conceivable that the vena caval narrowing will easily occur in the supine position in the human when he or she behaves to increase the pressure of the abdominal cavity. If the elevation of the pressure is relatively slight like a pressure less than 40 mmHg, the blood flow in the vena cava may be temporarily stopped at just the infradiaphragmatic portion, and therefore venous blood of the vena cava may enter the vertebral veins at the portion.
of upper lumbar vertebrae. When the pressure of the abdominal cavity is markedly elevated, the vena caval narrowing may occur along a longer part of vessels and the blood of the vena cava may enter the vertebral veins at the portion of lower lumbar vertebrae.

When the pressure of the abdominal cavity was elevated in the head-up tilt position in the dog in the present study, the narrowing of caudal vena cava was not observed; however, the blood flow in the vena cava became very slow and almost stopped. These findings were quite similar to phenomena previously reported and observed during a Valsalva maneuver in the human [16,18,19]. During the maneuver, when the venous blood of the inferior vena cava flows slowly or stops, the pressure of vena cava and atrial pressure shows about 15 cmH₂O (11 mmHg) and near 0 mmHg, respectively [19], the each pressure of intrathoracic and intraabdominal cavities is 40 mmHg, the venous blood of extracavity such as the subclavian and femoral veins is observed to flow into the vertebral veins [18,20], and the peripheral venous pressure increases to 30 to 50 mmHg [20]. In the head-up tilt position with an abdominal compression in the present study of the dog, when caudal vena caval blood entered the vertebral veins, the caudal vena caval pressure was 23.8 mmHg, which was about 14 mmHg higher than in the head-up position under relaxation. Intraabdominal pressure at this time was 39.2 mmHg, which was 7 mmHg higher than that in the supine position. In the human, the inferior vena caval pressure is approximately 20 mmHg when standing relaxed [21]. In our study, intraabdominal pressure in the human with abdominal contraction was 69.3 ± 19.8 mmHg in the sitting position and 73.8 ± 19.8 mmHg in the standing position. These high intraabdominal pressure values must be enough to cause inflow of the inferior vena caval blood into the vertebral veins.

In conclusion, venous drainage of the prostate gland into the vertebral vein system basically occurs when the blood flow from the abdominal vena cava to the thoracic vena cava is prevented. The disturbance of the blood flow in the vena cava induces an elevation of its venous pressure, and this phenomenon is strongly related with the elevation of intraabdominal pressure. And venous drainage into the vertebral veins may occur when intraabdominal pressure exceeds 32 mmHg in the supine position and 40 mmHg in the head-up tilt position. There are several routes for venous drainage from the prostate into the vertebral veins. The drainage will be observed mainly at the level of the rostral vertebrae when the elevation of intraabdominal pressure is relatively small in the supine position; however, it will be found around the caudal lumbar or sacral vertebrae during a marked elevation of the pressure in the supine position, head-up tilt or standing with abdominal muscle contraction. These findings suggest an important mechanism of hematogenous metastasis of the prostate cancer cells to the vertebral column.

REFERENCES

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