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ORIGINAL RESEARCH

Detection of the Vesical Arteries Using Three-dimensional Digital Subtraction Angiography Relevant to Intra-arterial Infusion Chemotherapy for Bladder Cancer Using Double-balloon Catheters

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Abstract:
Purpose: This study aims to assess and measure the origin of the superior vesical artery and its distance from the anterior trunk of the internal iliac artery, to which the anticancer drug is infused via double-balloon-occluded arterial infusion bladder-preserving therapy for locally invasive bladder cancer.
Material and Methods: The 160 pelvic sides of 80 patients were analyzed. Double-balloon catheters were bilaterally introduced into the contralateral superior gluteal artery via the internal iliac arteries using a bilateral transfemoral approach. The proximal balloon is placed at the internal iliac artery, proximally from superior gluteal artery bifurcation, whereas the distal balloon at the origin of the superior gluteal artery to isolate the anterior trunk of the internal iliac artery discharging to the targeted vesical arteries between the balloons. The side hole between the distal and proximal balloons was adjusted at the origin of the anterior trunk of the internal iliac artery to allow clear visualization of the angiographic flow into the bladder. After the distal and proximal balloons were inflated, three-dimensional rotational digital subtraction angiography was performed by simultaneous contrast injection from one extension tube connected to bilateral catheters. The distance (X) between the origins of anterior trunk of the internal iliac artery and superior vesical artery was measured on three-dimensional digital subtraction angiography images, and the origin of the inferior vesical artery was investigated.
Results: All superior vesical artery originated from anterior trunk of the internal iliac artery. The mean x was 7.2 mm (range 1.0-22.0 mm). All inferior vesical arterys branched from anterior trunk of the internal iliac artery or its branches.
Conclusions: Superior vesical artery commonly originates from the proximal portion of anterior trunk of the internal iliac artery close to superior gluteal artery bifurcation.

Keywords:
invasive bladder cancer, vesical artery, double-balloon catheter, double-balloon-occluded arterial infusion, three-dimensional digital subtraction angiography

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Introduction

The standard treatment for locally invasive bladder cancer has been radical cystectomy with pelvic lymph node dissection. However, approximately 50% of patients with invasive bladder cancer still die with the survival outcome closely related to its pathologic stage [1]. Additionally, the quality of life of patients is impaired by urinary diversion and impotence caused by total cystectomy. In our institution, the novel bladder preservation therapy known as the Osaka Medical College (OMC) regimen has resulted in a good clinical response [1-3]. This multimodality regimen comprises transurethral bladder tumor resection, systemic chemotherapy, radiation therapy, hemodialysis, and balloon-occluded arterial infusion (BOAI).

BOAI using a single-balloon catheter, so-called a single

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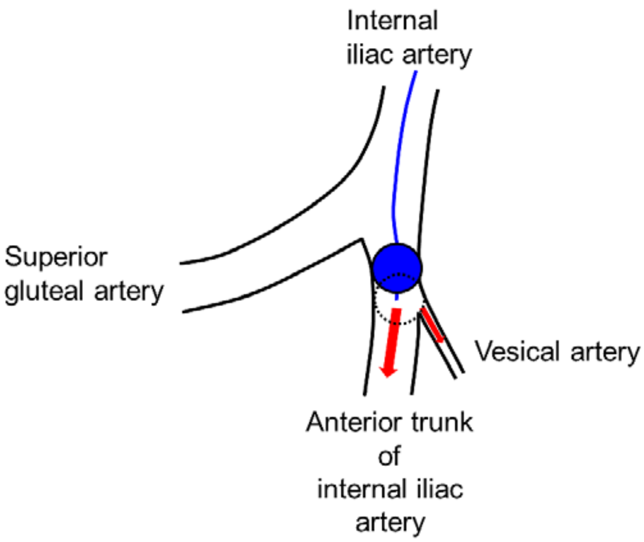

Figure 1. Schema of the most popular single-balloon-occluded arterial infusion technique. The balloon (round blue ball) is in the anterior trunk of the internal iliac artery downstream of the bifurcation of the superior gluteal artery. In this method, an anticancer drug cannot be infused into the vesical artery because the balloon could block its origin.

Table 1. Patients' Characteristics.

Characteristic	Data
Age in years, median (range)	68 (38–83)
Sex	
Male	64 (80)
Female	16 (20)
Clinical stage	
T-stage before TUR-Bt	
Tis	10 (12.5)
T1	8 (10)
T2	50 (62.5)
T3	10 (12.5)
T4	2 (2.5)
Tumor histology	
UC	
G1	2 (2.5)
G2	18 (22.5)
G3	54 (67.5)
Unknown	6 (7.5)

Data are presented as n (%) unless otherwise indicated.

TUR-Bt, transurethral resection of the bladder tumor; Tis, carcinoma *in situ*; UC, urothelial carcinoma

BOAI (S-BOAI) [4-6], commonly places the single-balloon at the origin of the anterior trunk of the internal iliac artery (AT-IIA), downstream from the bifurcation of the superior gluteal artery (SGA). However, if the SVA originates from the AT-IIA origin (**Fig. 1**), a concern is the balloon may occlude the origin of the superior vesical artery (SVA).

In contrast, BOAI as part of the OMC regimen uses an original four-lumen double-balloon (4L-DB) catheter. Here, the proximal balloon is placed at the internal iliac artery (IIA), proximallyfrom the SGA bifurcation. The distal balloon is placed at the origin of the SGA to isolate the AT-IIA discharging to the targeted vesical arteries (VAs) between the balloons. After placing the balloons in their proper sites, anticancer drugs (ADs) are infused via the side holes bilaterally and simultaneously. The 4L-DB catheter was devised on the basis of the vascular anatomy of the SVA often originating close to the AT-IIA origin and the inferior VA (IVA) originating from the AT-IIA or its branch.

Although some studies have evaluated the branches of the IIA including the IVA [7-15], there have been no published radiological or anatomical assessments of the origin of the SVA, especially its distance from the origin of the AT-IIA. In this retrospective study, we evaluated the site of SVA bifurcation by measuring the distance between the origins of the AT-IIA and VA. Additionally, we investigated the branching position of the IVA in the AT-IIA.

Material and Methods

Patients

This retrospective study was approved by the institutional review board of the Osaka Medical and Pharmaceutical University hospital. The requirement of informed consent for the use of the data about medical records and radiographic images was waived.

We performed double BOAI (D-BOAI) in patients with bladder cancer who underwent radical cystectomy from February 2016 to November 2017 and who wished to preserve bladder function. All patients were Asian. Eligible patients had histologically confirmed carcinoma *in situ* or stage T1, T2, T3, or T4 muscle-invasive bladder cancer without distant metastasis. 80 patients (64 men and 16 women; mean age 65.6 years, range 38-83 years) were enrolled and successfully analyzed using conventional two-dimensional DSA (2 D-DSA) and three-dimensional rotational DSA (3D-DSA) images. The clinical characteristics of the patients are presented in **Table 1**.

BOAI procedure and imaging protocol

For the infusion procedure, we used an intra-arterial 6-Fr catheter equipped with two occlusion balloons (M6F-28-70-TBSB4-ST; Terumo Clinical Supply Co., Ltd., Tokyo, Japan) (**Fig. 2**). Th 4L-DB catheter has four lumens. The first lumen leads to the tip hole for inserting the guidewire. The second lumen leads to the side hole between the two balloons for injecting the AD or contrast medium (CM). The third lumen is used to inflate the distal balloon. The fourth lumen is used to inflate the proximal balloon.

The catheters were bilaterally introduced into the posterior trunk of the IIA via the contralateral femoral artery using 7-Fr sheaths (RR-A70K25AL; Terumo Co., Ltd., Tokyo, Japan) and 0.025 guidewires (RF-GA25153; Terumo Co., Ltd., Tokyo, Japan). After the distal balloon had passed through the bifurcation of the AT-IIA, the distal and proximal balloons were inflated and immobilized to isolate the AT-IIA, which lies proximally from the target vessels (i.e., VAs) between the balloons (**Fig. 3**). We confirmed no visualization of SGA, no backflow into the proximal part of the IIA, and the preferential blood flow into the bladder with marked tumor stain using 2D-DSA. During the process of intra-arterial infusion chemotherapy as part of the OMC regimen, various amounts of cisplatin (100, 200, or 300 mg) were locally infused through both side holes between the distal and proximal balloons over a 1-h period. Before the intra-arterial infusion chemotherapy, we acquired both 2D-DSA and 3D-DSA images of D-BOAI.

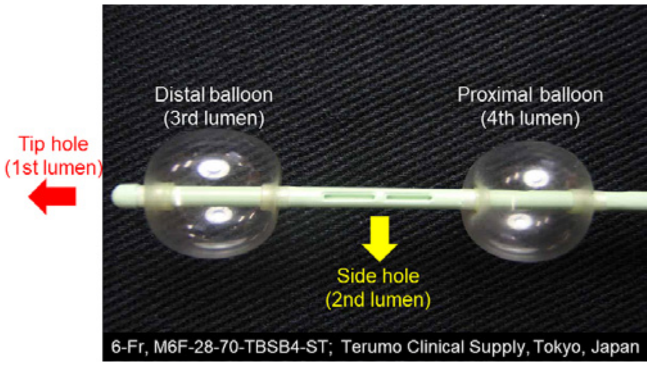

Figure 2. Four-lumen double-balloon catheter. The first lumen leads to the tip hole for inserting the guidewire. The second lumen leads to the side hole between the two balloons for injecting the anticancer drug or contrast medium. The third lumen is used to inflate the distal balloon. The fourth lumen is used to inflate the proximal balloon. The distance between the two balloons is 4 cm, and the inflated diameter of each balloon is 12 mm (reprinted from Ref. [15]. An Open Access article (CC BY 4.0).).

All angiograms were obtained using the same angiography equipment (Artis zee BA; Siemens AG, Erlangen, Germany) and the same injection parameters after bilateral catheters were connected to one high-pressure-resistant extension tube from a CM injector (Mark V ProVis Angiographic Injection System; Medrad, Inc., Warrendale, PA, USA). 2D-DSA was performed using the following parameters: 10 mL of iopamidol (370 mg I/mL) injected at a rate of 1.5 mL/s in an anteroposterior position at four frames per second. 3D-DSA was performed using the following parameters: 10 mL of iopamidol (370 mg I/mL) was injected at a rate of 1.5 mL/s, and 135 frames per second were obtained over a 200° rotation with the C-arm in the roll position. The images were automatically sent to the dedicated workstation, and a 3D volume was reconstructed within seconds of the acquisition. We mainly use the 3D-DSA images for the detection of SVA and IVA. In complex cases, we utilize preprocedural contrast-enhanced computed tomography (CT) angiography to evaluate the pelvic arterial tortuosity and stricture.

Data analysis

The 3D-DSA image data were transferred to a dedicated workstation (Syngo X Workplace; Siemens Healthcare, Erlangen, Germany). This workstation enables to provide 3D-DSA images from all directions and to separate the complicated overlap of many pelvic arteries. From the best view of

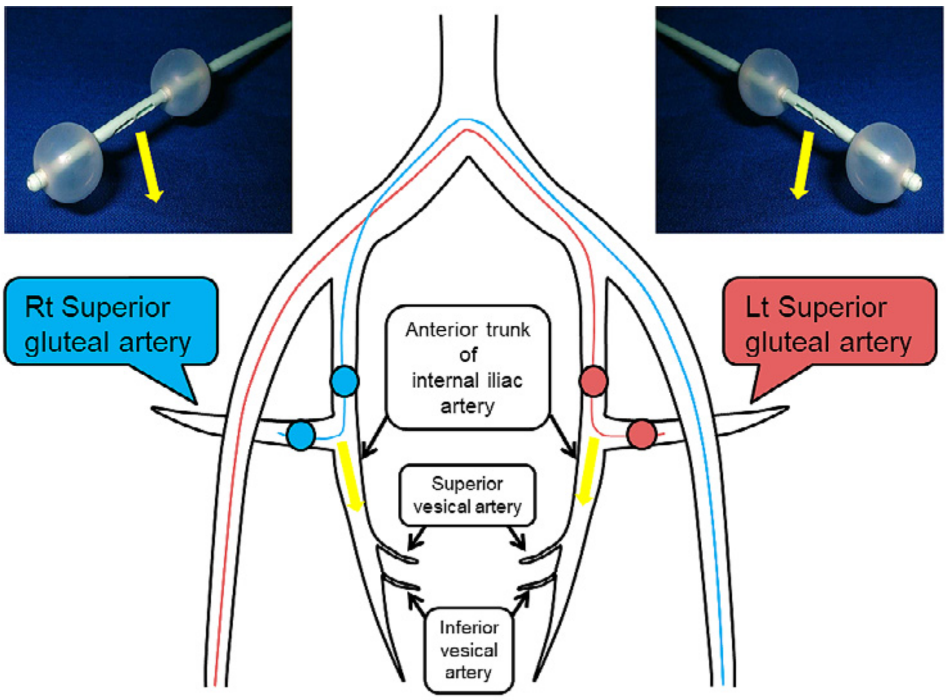

Figure 3. Schema of double-balloon-occluded arterial infusion. Double-balloon catheters (6 Fr) are introduced into the left (Lt) and right (Rt) superior gluteal arteries via the contralateral femoral arteries. Side holes between the distal and proximal balloons are placed to allow clear visualization of angiographic flow into the superior and inferior vesical arteries.

the 3D-DSA image, the origin of the SVA was assessed, and the distance (X) between the origin of the AT-IIA and the origin of the SVA was measured (**Fig. 4**). The SVA was defined as a first vessel branch that continues to the upper part of the bladder in the branches of the IIA.

Furthermore, we used 3D-DSA to identify which branch of the IIA the IVA originates from. For cases in which identification was difficult, preoperative contrast-enhanced CT angiography images were also used for evaluation. The IVA was defined as a blood vessel continuing to the lower part of the bladder among the branches of the IIA.

Results

The results of this study are shown in **Table 2** and **3**. The total average value of X was 7.2 mm (range 1.0-22.0 mm; right 7.3 mm and left 7.0 mm). The average values of X in men and women were 7.2 mm (range 1.0-22.0 mm; right 7.3 mm and left 7.2 mm) and 6.9 mm (range 1.7-12.2 mm; right 7.2 mm and left 6.7 mm), respectively. The frequency of SVA and IVA forming a common trunk was 39%. The most frequent origin of the IVA branching independently from the SVA was at the AT-IIA, and the frequency was 32%.

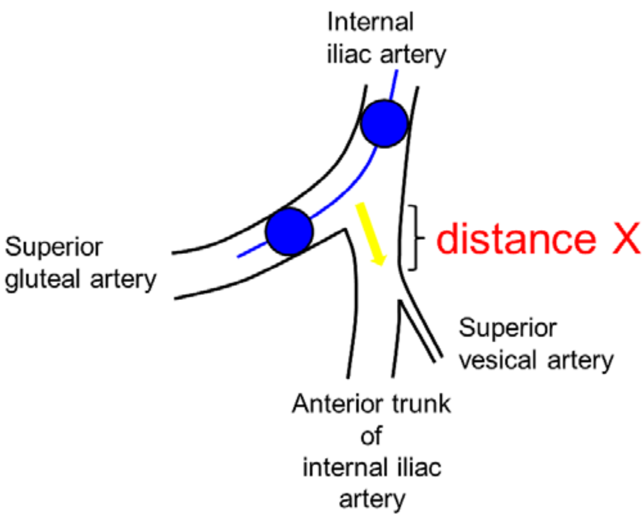

Figure 4. Schema of the anterior trunk of the internal iliac artery (AT-IIA) and superior vesical artery (SVA). In this study, we measured X, which is the distance between the branching point of the AT-IIA and the origin of the SVA.

Discussion

In the presence of bladder cancer, several feeding arteries—mainly the SVA and IVA—are present as branches of the IIA. Our study revealed that the SVA frequently originates from the proximal part of the AT-IIA, that the IVA originates from the AT-IIA, and that the SVA and IVA originate with common trunk in some cases. It is difficult to perform selective arterial infusion into each of these feeding arteries using a microcatheter. The BOAI method was then developed to perform hyperdense infusion into these many feeding arteries. It is presumed that the decreased blood pressure caused by balloon occlusion allows for delivering highly concentrated AD into the target arteries. Especially, our novel D-BOAI method enables preferential delivery of the AD into the tumor site under decreased blood pressure via proximal balloon occlusion without escape of AD into SGA via distal balloon occlusion.

The BOAI technique for treating intrapelvic malignant neoplasms was first suggested by Yamada et al. in 1981 [4]. Their method, which we called S-BOAI, used single-balloon catheters that temporarily occluded the bilateral IIAs. ADs were then infused from the end-hole of the catheters in the distal direction. Since then, other S-BOAI methods for bladder cancer have been developed [5, 6]. Although the method of S-BOAI has not yet been standardized, the most common method is S′-BOAI that we call for convenience. On S′-BOAI method, a single-balloon is placed in the AT-IIA downstream from the SGA bifurcation.

Theoretically, the S′-BOAI method seemed to be as effective as D-BOAI, because it is possible to deliver highly concentrated AD via the VA to the tumor site without infusing it into the SGA. However, as clarified in our study, most SVAs originate near the origin of the AT-IIA. Therefore, with the S′-BOAI method, the balloon may occlude the origin of the SVA and preclude efficient delivery of the AD into the tumor site.

In previous studies, 3D-DSA has been proven to be beneficial in the evaluation of intracranial or pelvic vascular anatomy [16-18]. Especially in the pelvic region, it may be difficult to separate the origin of the target arteries from many overlapped vessels on 2D-DSA images. In contrast, 3D-DSA images help in the detection of the origin of the SVA and precise measurement of the distance between the origins of the AT-IIA and SVA (**Fig. 5**).

Our study has several limitations. First, only 3D-DSA images were used to evaluate the arterial anatomy, and cone-

Table 2. The Distance (X) between the Branching Point of the Anterior Trunk of the Internal Iliac Artery and the Origin of the Superior Vesical Artery.

Participant	Mean ± SD (right)	Mean ± SD (left)	Mean ± SD (total)
Male (n = 64)	7.3 ± 3.4 (range: 1.2–21.0)	7.2 ± 3.7 (range: 1.0–22.0)	7.2 ± 3.6 (range: 1.0–22.0)
Female (n = 16)	7.2 ± 3.3 (range: 1.7–12.2)	6.7 ± 2.8 (range: 2.0–12.0)	6.9 ± 3.0 (range: 1.7–12.2)
Total (n = 80)	7.3 ± 3.3 (range: 1.2–21.0)	7.0 ± 3.6 (range: 1.0–22.0)	7.2 ± 3.4 (range: 1.0–22.0)

Data units are presented as millimeters unless otherwise indicated.
SD, standard deviation

Table 3. The Origin of the Inferior Vesical Artery in the Branches of the Internal Iliac Artery and the Frequency of Forming a Common Trunk with the Superior Vesical Artery.

	Right (n = 80)	Left (n = 80)	Total (n = 160)
Common trunk with SVA			
AT-IIA	31 (39)	32 (40)	63 (39)
Independent branch of SVA			
AT-IIA	27 (22)	25 (31)	52 (32)
IPA	14 (18)	13 (16)	27 (17)
OA	5 (4)	7 (9)	12 (8)
IGA	1 (1)	1 (1)	2 (1)
UA	2 (2)	2 (2)	4 (3)

Data are presented as n (%) unless otherwise indicated.

AT-IIA, anterior trunk of the internal iliac artery; SVA, superior vesical artery; IPA, internal pudendal artery; OA, obturator artery; IGA, internal gluteal artery; UA, umbilical artery

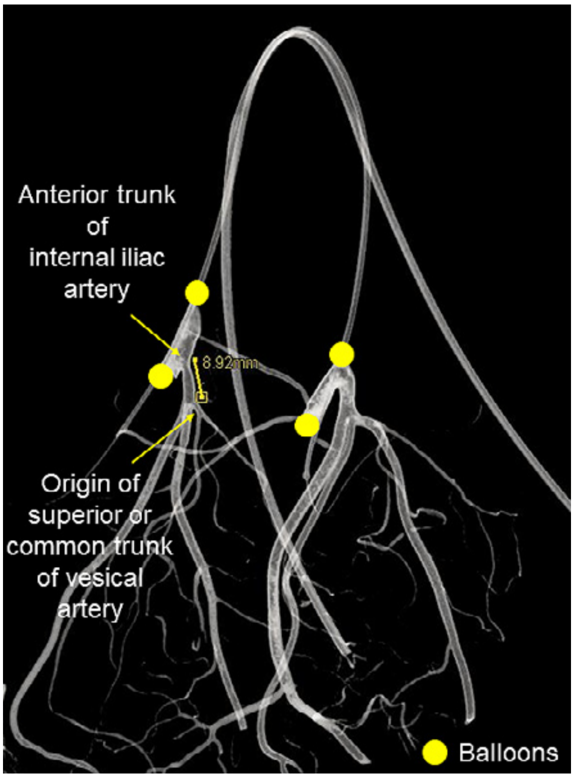

Figure 5. Three-dimensional rotational digital subtraction angiography (3D-DSA) of the internal iliac artery with double-balloon-occluded arterial infusion. Detection of the origin of the superior vesical artery (SVA) or the common trunk of the vesical artery was easier using 3D-DSA than using conventional DSA. Top arrow, anterior trunk of the internal iliac artery (AT-IIA); bottom arrow, origin of the SVA or the common trunk of the vesical artery; thin vertical line, the distance (X) between the branching point of the AT-IIA and the origin of the SVA or the common trunk of the vesical artery (8.92 mm).

beam CT was not performed. Some authors reported the usefulness of cone-beam CT for detecting pelvic arteries relevant to prostatic arterial embolization, but no reports have compared arterial detectability in 3D-DSA with that in cone-beam CT. Further evaluation with different imaging methods is necessary to confirm our data. Second, in this study, the SGA was blocked by a balloon, and then, this area was not evaluated using 3D-DSA. Therefore, whether the SVA is a variation that branches from the SGA cannot be evaluated in this study.

In conclusion, most VAs originated from the AT-IIA near the SGA bifurcation. The D-BOAI method enables to infuse the AD into the SVA and IVA from the AT-IIA.

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Conflict of Interest: None

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