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Table S1. Reasons for the lack of histological verification and the supporting evidence of venous tumor thrombus (VTT) in 26 cases.

Patient No	VTT type	Range of VTT (branches)	Reasons for the lack of histological verification	Evidence of VTT
1	1a	IIV	The primary tumor was huge and hard to excise. After removal of the tumor, the hemorrhage was great and there would be a risk of massive bleeding if keep resecting the VTT.	1. At presentation, the patient's D-dimmer value was normal. 2. Streak-like enhancement could be seen within the VTT. 3. The patient experienced local recurrence after surgery. Follow-up CT scan showed progression of the VTT within the same vein (IIV) with calcification within the venous lumen.
3	1a	IIV (peri-vertebral v.)	The same reason as patient 1.	The patient experienced local recurrence after surgery. Follow-up CT scan showed progression of the VTT within the same vein (IIV) with streak-like enhancement within the venous lumen.
6	1a	IIV	Not recorded in the operation note.	At presentation, the contrast CT scan showed calcification within the branches of IIV.
7	1a	IIV (presacral v.)	The VTT was located in the presacral venous plexus, which was too extensive to resect.	At presentation, the contrast CT scan showed calcification within the branches of IIV.
10	1b	EIV	Not recorded in the operation note.	1. At presentation, the patient's D-dimmer value was normal. 2. The caliber of the EIV was enlarged.
16	2a	CIV/IIV (gluteal/presacral v.)	The same reason as patient 1.	1. At presentation, the patient's D-dimmer value was normal. 2. At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.
17	2a	CIV/IIV (extensive branches/paravertebral/presacral/gluteal/visceral v.)	No operation	At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.
20	2a	CIV/IIV (presacral v.)	No operation	At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.

22	2a	CIV/IIV	The same reason as patient 1.	At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.
23	2a	CIV/IIV (gluteal v.)	The same reason as patient 1.	<ol style="list-style-type: none"> <li>1. The caliber of the CIV was enlarged.</li> <li>2. The patient was complicated by blend thrombus in the EIV. Under MRI scan, the characteristics of the thrombus in the CIV/IIV (isointense in T1WI, hyperintense in T2WI, hyperintense in dADC ) was different from that of the thrombus in the EIV (hyperintense in T1WI, hyperintense in T2WI, hypointense in dADC).</li> <li>3. Intraoperative inspection showed that the thrombus within the CIV/IIV was white and hard, while that within the EIV was black and soft.</li> </ol>
24	2a	CIV/IIV	Not recorded in the operation note.	<ol style="list-style-type: none"> <li>1. At presentation, the patient's D-dimmer value was normal.</li> <li>2. At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.</li> </ol>
25	2a	CIV/IIV (presacral v.)	Not recorded in the operation note.	<ol style="list-style-type: none"> <li>1. At presentation, the patient's D-dimmer value was normal.</li> <li>2. At presentation, the contrast CT scan showed calcification within the branches of IIV and CIV.</li> </ol>
26	2a	CIV/IIV (gluteal v.)	The same reason as patient 1.	<ol style="list-style-type: none"> <li>1. At presentation, the patient's D-dimmer value was normal.</li> <li>2. The patient experienced local recurrence after surgery. Follow-up CT scan showed progression of the VTT within the same vein (CIV) with streak-like enhancement within the venous lumen.</li> </ol>
27	2c	CIV/EIV/IIV (extensive branches/Corona Mortis v./obturator v.)	Not recorded in the operation note.	At presentation, the contrast CT scan showed calcification within the venous system.
29	2c	CIV/EIV/IIV (gluteal/presacral v.)	No operation	<ol style="list-style-type: none"> <li>1. At presentation, the caliber of the CIV was enlarged.</li> <li>2. The VTT had the same characteristics as the primary tumor in MRI scan.</li> </ol>
30	2c	CIV/EIV/IIV (gluteal v.)	No operation	The VTT had the same characteristics as the primary tumor in MRI scan.
32	3a	IVC(below RV)/CIV/IIV (gluteal v.)	The same reason as patient 1.	At presentation, the contrast CT scan showed streak-like enhancement within the venous lumen.
33	3a	IVC(below RV)/CIV/IIV	The same reason as patient 1.	At presentation, the contrast CT scan showed enlarged caliber of the IVC/CIV and streak-like

				enhancement within the venous lumen.
34	3a	IVC(below RV)/CIV/IIV (presacral v.)	The same reason as patient 1.	At presentation, the contrast CT and MRI scan showed enlarged caliber of the IVC/CIV and streak-like enhancement within the venous lumen.
37	3a	IVC(below RV)/CIV/IIV	Not recorded in the operation note.	At presentation, the contrast MRI scan showed enlarged caliber of the IVC/CIV and enhancement within the venous lumen.
38	3b	IVC(below RV)/CIV/EIV	The same reason as patient 1.	At presentation, the contrast CT and MRI scan showed streak-like enhancement within the venous lumen.
39	3c	IVC(below RV)/CIV/EIV/IIV (Corona Mortis v./obturator v.)	Not recorded in the operation note.	1. The caliber of the EIV/CIV was enlarged. 2. The patient experienced local recurrence after surgery. Follow-up CT scan showed progression of the VTT that grew into the contralateral CIV.
40	4a	IVC(below RV)/bil. CIV/right IIV	No operation	At presentation, the contrast MRI scan showed enlarged caliber of the IVC/CIV/IIV and enhancement within the venous lumen.
41	4a	Bil. CIV/Left IIV (presacral v.)	The VTT was too extensive to excise.	1. At presentation, the patient's D-dimmer value was normal. 2. At presentation, the contrast CT scan showed streak-like enhancement within the venous lumen.
43	4a	IVC (below RV)/bil. CIV & IIV (presacral v.)	The VTT was too extensive to excise.	1. At presentation, the caliber of the IVC/CIV was enlarged. 2. PET/CT scan showed high metabolic activity within the venous lumen.
44	4b	IVC(above RV)/bil. CIV/right EIV & IIV	No operation	1. At presentation, the contrast CT showed enlarged caliber of the IVC/CIV and calcification within the venous lumen. 2. At presentation, the contrast MRI scan showed enlarged caliber of the IVC/CIV and streak-like enhancement within the venous lumen.

Abbreviation: V.-vein, contral.-contralateral, ipsil.-ipsilateral, bil.-bilateral, IIV-internal iliac vein, EIV-external iliac vein, CIV-common iliac vein, IVC- inferior vena cava, v.-vein, RV-renal vein.

Table S2. Details of 44 cases with venous tumor thrombus

No	Age/ sex	Stage (meta.)	Diagnosis (subtype)	Invasion of anatomical landmark	Extent of Sacral invasion	Type of resection	VTT type	Range of VTT (branches)	DV T	Chemotherap y	Response to chemotherapy -primary tumor*	Response to chemotherapy -VTT *	Operation for tumor/VTT	F.U. (mths)/ status
1	15M	III (lung)	OS (chondro.)	G.S.F.	Contral. ala	I/II/IV	1a	IIV		Yes	SD	SD	L.S./N	7/D
2	18F	IIB	OS (chondro.)	O.F.	Ipsil. ala	I/II/III/IV	1a	IIV (gluteal v.)		Yes	PD	SD	L.S./resection	13/A
3	19M	III (bone)	OS (chondro.)	G.S.F. L5/S1 I.F.	Sacral foramina	I/IV	1a	IIV (peri-vertebral v.)		No	/	/	L.S./N	6/A
4	23M	IIB	OS (chondro.)	Lumbar canal	Contral. ala	I/II/III/IV	1a	IIV (presacral v.)		Yes	SD	SD	L.S./partial resection	10/D
5	27M	IIB	CS (dediffer.)	G.S.F.	Sacral foramina	I/II/IV	1a	IIV (gluteal/presacral v.)		No	/	/	L.S./resection	LTF
6	29M	III (lung)	OS (NOS)		Ipsil. ala	I/II/III/IV	1a	IIV		Yes	SD	SD	L.S./N	15/NE
7	33F	IIB	OS (osteo.)	G.S.F. O.F. L5/S1 I.F.	Contral. ala	I/II/III/IV/PF	1a	IIV (presacral v.)		Yes	SD	SD	L.S./N	16/D
8	58M	IIB	UPS	Psoas G.S.F.	Ipsil. ala	I/II/IV	1a	IIV (gluteal v.)	Yes	Yes	SD	SD	L.S./resection	24/D
9	19M	IIB	OS (small cell)	Psoas O.F.	None	II/III	1b	EIV		Yes	SD	SD	L.S./ thrombectomy	26/A

10	29M	III (lung)	OS (chondro.)	O.F.	None	II/III	1b	EIV	No	/	/	L.S./N	LTF
11	9M	III (lung)	OS (chondro.)		Ipsil. ala	I/II/IV	1b	EIV	Yes	SD	SD	L.S./ thrombectomy	6/D
12	12F	IIA	EWS		None	II/III	1c	EIV/IIV (Corona Mortis v./obturator v.)	No	/	/	L.S./ thrombectomy	26/NE
13	21F	IIB	OS (fibro.)	O.F.	None	II/III	1c	EIV/IIV (extensive branches/Corona Mortis v./obturator v.)	No	/	/	L.S./resection	11/NE
14	32F	III (lung, bone)	OS (chondro.)	G.S.F. O.F. Lumbar canal L5/S1 I.F.	Canal	I/II/III/IV/PF	1c	EIV/IIV (Extensive branches/Corona Mortis v./obturator /pudental/presacral v.)	Yes	SD	SD	L.S./ thrombectomy	14/A
15	48F	IIB	OS (NOS)		None	I/II/III	1c	EIV/IIV (Corona Mortis v./obturator v.)	No	/	/	L.S./ thrombectomy	42/A
16	14M	III (lung)	OS (osteo.)	G.S.F. Lumbar canal L5/S1 I.F.	Contral. ala	I/IV	2a	CIV/IIV (gluteal/presacral v.)	Yes	PD	SD	L.S./N	10/D
17	15M	III (lung)	OS (NOS)	L5/S1 I.F.	Sacral foramina	I/II/IV	2a	CIV/IIV (extensive branches/paravertebral/pre sacral/gluteal/visceral v.)	Yes	PD	SD	No operation	8/D
18	15M	IIB	OS (chondro.)	G.S.F. L5/S1 I.F.	Ipsil. ala	I/II/IV	2a	CIV/IIV (gluteal/presacral v.)	Yes	SD	PD	L.S./partial resection	11/D
19	19M	III (lung)	OS (chondro.)	G.S.F. O.F.	Sacral foramina	I/II/III/IV	2a	CIV/IIV	Yes	PD	SD	AP./resection	14/A

20	20M	IIB	OS (chondro.)	G.S.F. L5/S1 I.F.	Sacral foramina	I/II/III/IV	2a	CIV/IIV (presacral v.)	Yes	PD	PD	No operation	7/D	
21	26M	IIB	OS (osteo.)	L5/S1 I.F.	Sacral foramina	I/II/IV	2a	CIV/IIV (gluteal/presacral v.)	Yes	Yes	PR	SD	L.S./ thrombectomy	LTF
22	27M	IIB	OS (chondro.)	Lumbar canal L5/S1 I.F.	Canal	I/IV	2a	CIV/IIV	Yes	PD	PD	L.S./N	LTF	
23	33M	III (lung)	OS (chondro.)		Ipsil. ala	I/II/III/IV	2a	CIV/IIV (gluteal v.)	Yes	Yes	PD	SD	L.S./N	8/A
24	45M	IIB	CS (mesenchy mal)		Ipsil. ala	I/II/III/IV	2a	CIV/IIV	No	/	/	L.S./N	LTF	
25	52F	III (lung)	OS (osteo.)	Lumbar canal	Canal	I/II/III/IV	2a	CIV/IIV (presacral v.)	No	/	/	L.S./N	4/A	
26	57F	IIB	CS (dediffer.)		Sacral foramina	I/II/IV	2a	CIV/IIV (gluteal v.)	No	/	/	L.S./N	6/D	
27	21F	III (lung)	OS (osteo.)	G.S.F. O.F.	None	II/III	2c	CIV/EIV/IIV (extensive branches/Corona Mortis v./obturator v.)	Yes	Yes	SD	SD	L.S./N	12/D
28	22F	IIB	OS (chondro.)	Lumbar canal L5/S1 I.F.	Canal	I/II/III/IV	2c	CIV/EIV/IIV (gluteal/presacral v.)	Yes	SD	SD	L.S./resection	14/D	
29	30M	IIB	CS (grade III)	Psoas G.S.F. Lumbar canal L5/S1 I.F.	Contral. ala	I/II/IV	2c	CIV/EIV/IIV (gluteal/presacral v.)	No	/	/	No operation	LTF	

30	43M	III (lung)	Sarcoma	Psoas G.S.F.	Contral. ala	I/II/III/IV	2c	CIV/EIV/IIV (gluteal v.)	No	/	/	No operation	3/D	
31	12F	IIB	OS (chondro.)	G.S.F. O.F.	Ipsil. ala	I/II/III/IV	3a	IVC (below RV)/CIV/IIV (gluteal/presacral v.)	Yes	PR	SD	L.S./ thrombectomy	25/D	
32	16M	IIB	CS (mesenchy mal)	G.S.F.	Ipsil. ala	I/II/IV	3a	IVC(below RV)/CIV/IIV (gluteal v.)	No	/	/	L.S./N	6/A	
33	19M	IIB	OS (chondro.)	Psoas	Sacral foramina	I/IV	3a	IVC(below RV)/CIV/IIV	Yes	SD	SD	L.S./N	9/D	
34	21M	IIB	OS (chondro.)	L5/S1 I.F.	Canal	I/II/III/IV	3a	IVC(below RV)/CIV/IIV (presacral v.)	Yes	No	/	/	L.S./N	22/D
35	30M	IIB	CS (dediffer.)	L5/S1 I.F.	Canal	I/IV	3a	IVC(below RV)/CIV/IIV (presacral v.)	Yes	SD	SD	L.S./ thrombectomy	35/D	
36	31M	IIB	OS (NOS)	L5/S1 I.F.	Sacral foramina	I/IV	3a	IVC(below RV)/CIV/IIV (presacral v.)	Yes	Yes	PR	PR	L.S./partial resection	22/D
37	39F	IIB	MGCT	L5/S1 I.F.	Contral. ala	I/IV	3a	IVC(below RV)/CIV/IIV	Yes	No	/	/	L.S./N	4/A
38	28F	IIB	OS (chondro.)		Sacral foramina	I/IV	3b	IVC(below RV)/CIV/EIV	Yes	PR	PR	L.S./N	12/NE	
39	28F	IIB	OS (chondro.)		None	II/III	3c	IVC(below RV)/CIV/EIV/IIV (Corona Mortis v./obturator v.)	Yes	No	/	/	L.S./N	11/D
40	40F	IIB	Sarcoma	L5/S1 I.F.	Contral. ala	I/IV	4a	IVC(below RV)/bil. CIV/right IIV	No	/	/	No operation	6/D	
41	47F	III	CS		Contral.	I/II/III/IV	4a	Bil. CIV/Left IIV	No	/	/	L.S./N	8/A	

		(bone)	(mesenchy- mal)		ala			(presacral v.)						
42	14M	IIB	OS (chondro.)	O.F. Lumbar canal L5/S1 I.F.	Canal	I/II/III/IV	4a	Bil. CIV/right EIV&IIV/left IIV (peri-vertebral v.)	Yes		SD	SD	L.S./partial resection	13/A
43	27F	III (bone)	OS (chondro.)	Lumbar canal L5/S1 I.F.	Canal	I/IV	4a	IVC (below RV)/bil. CIV & IIV (presacral v.)	Yes	Yes	PD	PD	L.S./N	10/D
44	23F	IIB	Sarcoma	G.S.F.	Ipsil. ala	I/II/IV	4b	IVC(above RV)/bil. CIV/right EIV & IIV	Yes		PD	SD	No operation	7/D

Abbreviation: meta.-metastasis, VTT-venous tumor thrombus, DVT-deep vein thrombus, F.U.-follow up, mths-months, M-male, F-female, OS-osteosarcoma, CS-chondrosarcoma, chondro.-chondroblastic, osteo.-osteoblastic, fibro.-fibroblastic, dediffer.-dedifferentiated, NOS-not otherwise specified, UPS-undifferentiated pleomorphic sarcoma, EWS-Ewing sarcoma, MGCT- malignant giant cell tumor, G.S.F.-Invasion of the greater sciatic foramen, O.F.-Invasion of the obturator foramen, L5/S1 I.F.- invasion of the L5/S1 intervertebral foramen, contral.-contralateral, ipsil.-ipsilateral, bil.-bilateral, IIV-internal iliac vein, EIV-external iliac vein, CIV-common iliac vein, IVC- inferior vena cava, v.-vein, RV-renal vein, PF-proximal femur, L.S.-limb salvage, A.P.-amputation, N-no specific management, D-died of disease, A-alive with disease, NE-no evidence of disease, LTF-loss to follow-up, PR-partial response, SD-stable disease, PD-progressive disease.

\*: By the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.



Table S3. Survival analysis (log-rank test) of cases of osteosarcoma treated with surgery

Variables	Median survival (months, 95% CI)		P value
	Without VTT	With VTT	
Whole group (N=119)	N=93	N=26	
Overall survival	54.0 (25.6, 82.4)	16.3 (7.2, 25.3)	0.002
Recurrence-free survival	28.8 (19.0, 38.6)	15.0 (3.5,26.6)	0.008
Metastasis (progression)-free survival	32.3 (16.0, 48.6)	5.7 (1.6, 9.8)	<0.001
Non-metastatic diseases (N=91)	N=76	N=15	
Overall survival	54.0 (39.0, 69.0)	21.5 (10.8, 32.2)	0.003
Recurrence-free survival	32.4 (20.1, 44.7)	18.6 (6.1, 31.1)	0.020
Metastasis-free survival	41.0 (25.6, 56.4)	11.2 (1.4, 21.0)	<0.001
Metastatic diseases (N=28)	N=17	N=11	
Overall survival	12.3 (4.1, 20.5)	12.5 (9.2, 15.8)	0.779
Recurrence-free survival	8.9 (2.4, 15.3)	5.7 (1.4, 10.0)	0.637
Metastasis progression-free survival	8.3 (2.9, 13.8)	3.5 (0, 6.8)	0.133

Abbreviation: VTT- venous tumor thrombus

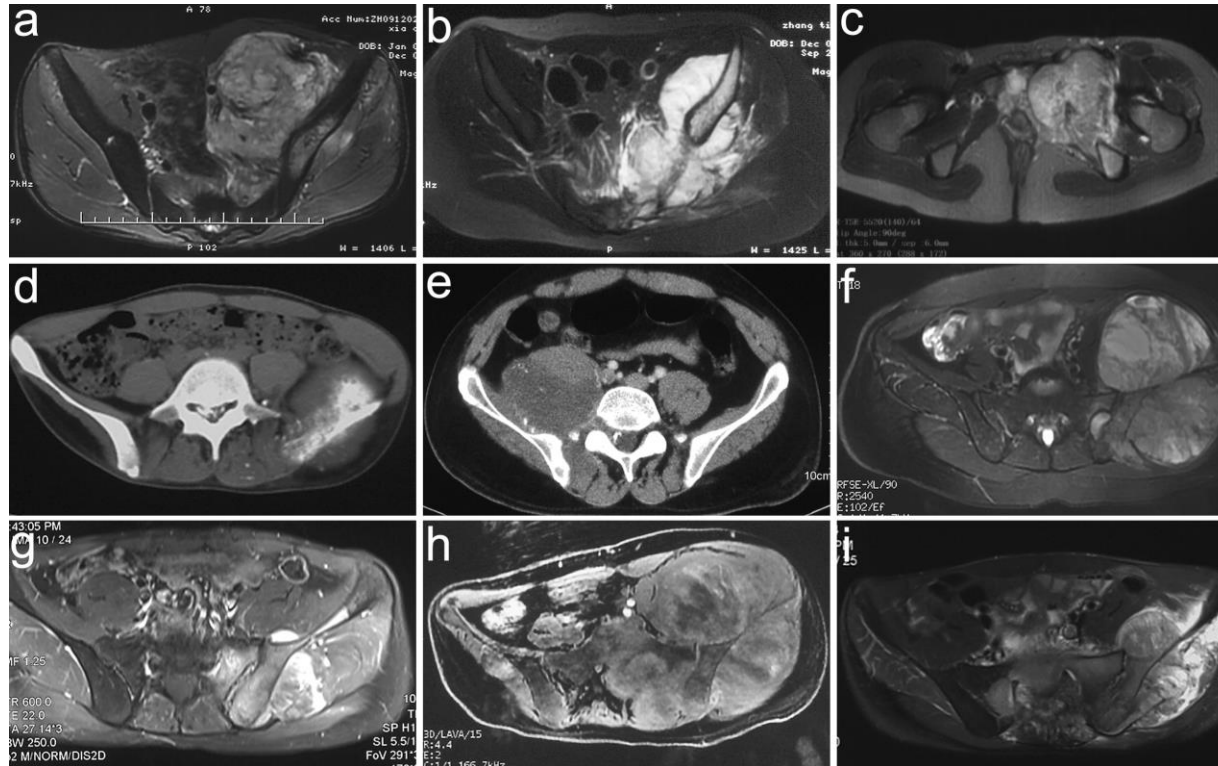


Figure S1. Illustration of the invasion of some anatomic landmarks.

- (a) Tumor replacement of the psoas. The tumor of the ilium with a huge mass invaded and erased the psoas. MRI showed that the psoas disappeared, and the tumor touched the external iliac vessels directly. We assumed that this situation might increase the risk of venous invasion by the tumor.
- (b) Invasion of the greater sciatic foramen. The tumor located around the sciatic notch with a huge mass would extend to the greater sciatic foramen and occlude the supra-/infra-pyiform foramina. We assumed that in this situation the tumor might be more likely to invade the gluteal veins and then to extend proximally.
- (c) Invasion of the obturator foramen. The tumor was derived from the puboischium region with a huge mass that located across the obturator foramen. We assumed

that in this situation, the tumor would be more likely to access the obturator vein or Corona-Mortis vein.

(d) Invasion of the lumbar spinal canal. The tumor extended to the L5 canal showing ossification in the epidural space.

(e) Invasion of the L5/S1 intervertebral foramen. The tumor located at the sacroiliac joint has extended to the L5/S1 intervertebral foramen. Noted that there was tumor thrombus within the right common iliac vein.

(f-i) Different extent of horizontal extension to the sacrum: (f) ipsilateral sacral ala, (g)-ipsilateral sacral foramina, (h)-midline/sacral canal, (i)contralateral ala. Different extent of sacral invasion might confer different risks of venous invasion.

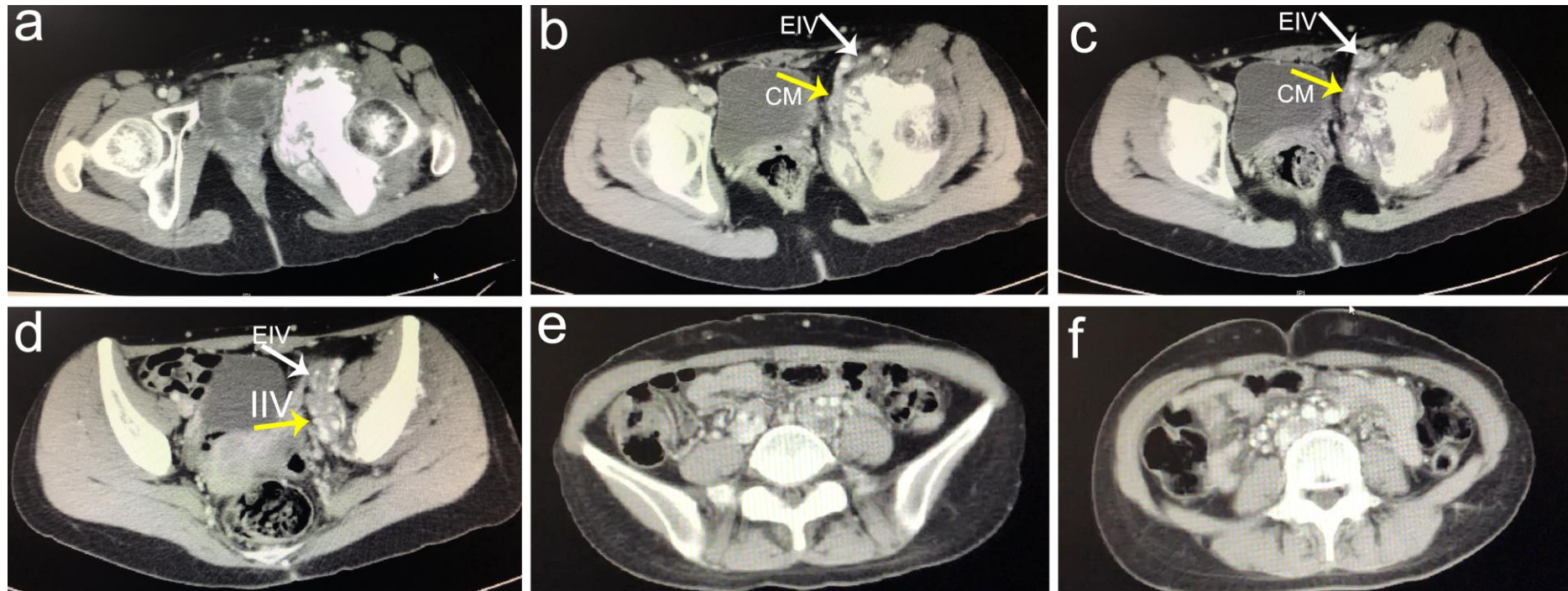


Figure S2. Illustration of the association between invasion of obturator foramen and development of venous tumor thrombus (VTT).

(a) This was a 29-year-old female with a type II/III pelvic osteosarcoma (chondroblastic subtype) with invasion of obturator foramen. The patient presented a type 3c VTT involving inferior vena cava, left common iliac vein, left internal and external iliac veins. (b-d) Axial images showed the VTT invading the external iliac vein (EIV), Corona-Mortis vein (CM), internal iliac vein (IIV). Intraoperative exploration confirmed that the VTT originated from the obturator vein and then extended both into the trunk of the internal iliac vein and into the external iliac vein through the Corona-Mortis vein.