1 Two-step arterial reconstruction technique for *en bloc* resection of a large retroperitoneal

2 liposarcoma involving the common iliac artery

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1 Abstract

2	Retroperitoneal liposarcoma (RPLS) is a rare but challenging neoplasm, which is frequently
3	associated with iliac vessel invasion. We describe how we used a two-step arterial reconstruction
4	technique to perform en bloc resection of a large RPLS involving the iliac arteries in three patients. A
5	temporal long in situ graft bypass was established using a prosthetic vascular graft during dissection
6	of the tumor. This bypass provided a unobscured surgical field, while maintaining blood flow in the
7	lower limb during the operation. After removal of the tumor, the new prosthetic vascular graft of a
8	suitable length was placed after washing out the abdominal cavity. No graft-related complications,
9	including vascular graft infection or graft occlusion, occurred during the follow-up period. This
10	novel technique appears to provide a safe and useful way to remove large RPLSs involving the
11	retroperitoneal major vessels.

1 Introduction

Retroperitoneal liposarcoma (RPLS) is difficult to diagnose at an early stage because characteristic 2 3 symptoms rarely appear (1). Therefore, RPLS tends to manifest as a large tumor with involvement of the major vessels in the retroperitoneal space, where the inferior vena cava, the abdominal aorta, and 4 5 the iliac arteries and veins are located (2, 3). A large tumor involving the arterial system is generally 6 regarded as locally unresectable disease because the surgical procedure is technically demanding and 7 requires a multidisciplinary surgical approach with the participation of oncological and vascular 8 surgeons. Nevertheless, an aggressive surgical approach to the treatment of a large RPLS should be 9 considered for selected patients because there is no clear evidence of the benefit of chemotherapy or radiotherapy for this tumor. 10 11 For a large RPLS involving the common iliac artery (CIA), arterial reconstruction from the CIA 12 to the external iliac artery (EIA) or the femoral artery (FA) to the lower extremity after arterial 13 resection is mandatory to prevent leg ischemia. However, arterial reconstruction is difficult in such cases because a large RPLS hanging over the CIA obscures the surgical field required for arterial 14 reconstruction. As an alternative procedure, non-in situ (non-anatomical) reconstruction, including 15 16 femoro-femoral bypass or axillo-femoral bypass on the tumor side, may be recommended. However, 17 in these procedures, the subcutaneous route of the graft bypass restricts the skin incision and prevents a clear surgical field. Moreover, the long-term patency of extra-anatomical bypass is inferior to that 18 19 of anatomical bypass (4). Therefore, an extra-anatomical bypass is not recommended, especially in

1	young	patients.

2	To overcome these drawbacks, we established a "two-step arterial reconstruction technique". In
3	this technique, a long bypass is temporarily established using an expanded polytetrafluoroethylene
4	(ePTFE) vascular graft as the first step. A suitable length of the new ePTFE vascular graft is applied
5	after tumor removal.
6	
7	Ethical considerations
8	This study was approved by the Ethics Committee of Nagoya University Hospital (approval No.
9	22803). Informed consent was obtained from all patients.
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12 13 14 15 16	A large RPLS involving the ipsilateral CIA was diagnosed in three patients (two men and one woman) at Nagoya University Hospital (Fig. 1). Two patients (patients #1 and #2) had deep vein thrombosis (DVT) and were treated with an anticoagulation drug before surgery. All surgeries were performed by teams of oncological surgeons and vascular surgeons at Nagoya University Hospital.

1	xiphoid to the pubis. A second abdominal transverse incision was made on the tumor side to expose
2	the entire tumor. Most of the portion of the small intestine that was not involved was inserted into a
3	plastic bag and retracted toward the contralateral side of the tumor. Subsequently, the tumor was
4	mobilized from the retroperitoneal space as much as possible. The involved organs, such as the
5	kidney, ureter, ovary, and large intestine, were resected in combination with the tumor, as necessary.
6	Moreover, as much as possible of the adjacent fat tissue in the retroperitoneal space was removed,
7	irrespective of the location of the tumor, to prevent local recurrence in the remnant fat tissue (so-
8	called compartment resection) (5). If the tumor had invaded the iliopsoas muscle, the diaphragm
9	and/or the femoral nerves, the invaded portion was resected to achieve a negative surgical margin.
10	The CIA at the proximal side of the tumor and the EIA or FA at the distal side of the tumor were
11	isolated and taped (Figs 2a and 2b). The internal iliac artery (IIA) was isolated and ligated to prevent
12	backflow from the pelvic organs before arterial resection and reconstruction. In one patient, the IIA
13	on the ipsilateral side was embolized using coils before surgery because the tumor received extensive
14	blood flow from the IIA. Isolation of the common iliac vein (CIV) and the internal iliac vein (IIV) is
15	recommended, but this preparation is sometimes made difficult by the presence of a large tumor.
16	Only the external iliac vein (EIV) at the distal side of the tumor was able to be isolated in all three of
17	the patients in this study. An activated clotting time (ACT) of > 200-250 seconds was maintained
18	with heparin infusion (3,000 IU per body) to prevent thrombus formation in the lower extremity
19	during arterial clamping (the ACT was monitored every 30-45 min). Following the application of

1	angled vascular clamps to the CIA and EIA/FA, these arteries were dissected approximately 1 cm
2	apart from the edge of the tumor. A long temporal bypass was created during en bloc resection of the
3	RPLS to maintain blood flow in the lower limb. In the first step of the anastomosis, we used a ringed
4	heparin-coated ePTFE (GORE [®] PROPATEN [®]) in two patients (patient #1 and #3) and a ringed non-
5	heparin-coated ePTFE (FUSION [®]) in the other patient (patient #2) for the anastomosis to the
6	EIA/FA. The distal clamp was then released momentarily to allow us to check the suture line for
7	hemostasis and to flush away any clotting in the graft. Subsequently, the graft was anastomosed to
8	the CIA (Fig. 2c). After the first-stage of the revascularization, the CIV, IIV, and EIV, as well as the
9	CIA and the EIA/FA, were divided; then, the large RPLS was safely removed en bloc from the
10	invaded retroperitoneal space with a clear surgical view. There was no need for restoration of these
11	veins (Fig. 2d). After resection of the tumor, the surgical field was rinsed thoroughly with more than
12	3 L of saline. In the second step of the anastomosis, the prosthetic vascular graft was adjusted to a
13	suitable length (Fig. 2e). The graft was wrapped securely with the greater omentum to prevent
14	contamination by intestinal bacteria (Fig. 2f). Colostomy was performed after skin closure in all
15	patients, who were also fitted with elastic stockings to prevent edema of the ipsilateral leg and DVT
16	after surgery. No anticoagulants were administered after surgery.
17	

Outcomes

19 The preoperative diagnosis was dedifferentiated liposarcoma (DD-LPS) in all patients and the

1	maximum tumor size was 18-35 cm (Table 1). All patients underwent combined colon resection and
2	two required ipsilateral kidney resection. None of the three patients required resection of the femoral
3	nerve. One patient (patient #2) had undergone tumor resection combined with colectomy and
4	nephrectomy for the primary tumor in another hospital 5 years prior to the surgery at Nagoya
5	University Hospital.
6	The temporal graft was 50-70 cm long and the final <i>in situ</i> graft was 8-13 cm long. The time
7	required to perform graft anastomosis in both the first and second steps was approximately 30 min.
8	The pathological diagnosis was DD-LPS in two patients and well-differentiated liposarcoma in one
9	patient. Two patients underwent macroscopic complete resection (R0/1). One patient did not undergo
10	complete resection because the tumor had invaded the sacroiliac joint and there was a small remnant
11	of the tumor in this location.
12	There was no incidence of thrombosis in the arterial graft or of ischemia of the lower limb
13	during the follow-up period. DVT developed in one patient (patient #3), who was treated with an
14	anticoagulation drug. Surgical site infection developed in two patients and was treated successfully
15	during the hospital stay. There were no deaths after surgery. For the patient who was not able to
16	undergo macroscopic complete resection, the remnant tumor was treated with proton therapy, and the
17	disease was well controlled thereafter for 16 months. The other patients showed no evidence of local
18	recurrence or distant metastasis during the follow-up period (range, 200-466 days), but one patient
19	died of another disease 200 days after surgery.

2 **Discussion**

3 Establishing the best surgical approach to a large RPLS involving the major vessels in the retroperitoneal space is challenging because of the limited information available on this rare tumor. 4 5 Only four cohort studies involving arterial resection during tumor resection in the retroperitoneal 6 space have been published (6-9). These studies reported that combined resection of soft tissue sarcoma was able to be performed with acceptable morbidity, including vascular graft patency and 7 8 favorable disease-specific survival. However, they did not provide suggestions or guidance on he 9 arterial reconstruction technique. One of the serious problems with surgical removal of a large RPLS 10 relates to the difficulty in maintaining a sufficient surgical view while dissecting a large tumor that 11 involves the major arteries. The other concern is the long period of ischemia that the lower limb is 12 subjected to during arterial resection and reconstruction. Our two-step arterial reconstruction 13 technique is useful not only for maintaining a sufficient surgical field, but also for preventing ischemia of the lower extremity while performing *en bloc* tumor resection. This technique may 14 15 enable us to perform safe en bloc resection of a large tumor involving the CIA. 16 In addition to this two-step technique, there is another option in which extra-anatomical 17 bypass is used to maintain the blood flow in the lower extremity, utilizing femoro-femoral bypass or 18 axillo-femoral bypass. These procedures are highly effective for preventing prosthetic graft infection; 19 however, there are two problems with the use of extra-anatomical bypass in patients with large

1	RPLSs. First, the subcutaneous route used for this bypass overlaps with the large skin incision
2	required. In fact, the three patients in the current study required large midline skin incisions featuring
3	a wide transverse incision on the tumor side to fully expose their large tumors. Second, the 5-year
4	graft patency rates of femoro-femoral and axillo-femoral bypasses using prosthetic vascular grafts
5	are reported to be 65% and 71.5%, respectively (10) (11), whereas that of anatomical bypass is
6	85.3% (12). Graft patency rates are clinically important in RPLS management because some patients
7	are young and may live long after surgery. Therefore, anatomical bypass should be used as often as
8	possible, especially in young patients, unless the surgical field is highly contaminated.
9	A long period of ischemia of the lower limb may result in not only ischemic complications,
10	including neuropathy or paresis, but it may also induce reperfusion injuries such as myonephropathic
11	metabolic syndrome (13). Therefore, the period of ischemia must be minimized and should not
12	exceed a few hours (14). However, large RPLSs sometimes invade the adjacent organs extensively,
13	encumbering mobilization of the tumor from the retroperitoneal space. In this difficult setting, the
14	required time for en bloc resection, being the ischemic interval, is unpredictable. In the present
15	series, it ranged from 147 to 413 min. This means that ischemic complications of the lower limb
16	might have occurred had the usual one-step vascular graft been performed. Fortunately, there were
17	no ischemia-related complications in this series, suggesting the utility and safety of the present two-
18	step approach. The two-step anastomosis required approximately 65 min, which was twice the
19	amount of time required for one-step arterial anastomosis.

1	In conclusion, we reported a novel technique for en bloc resection of large RPLSs involving
2	the iliac artery. This technique provides an adequately clear surgical field while maintaining blood
3	flow in the lower extremity during dissection of a large tumor in the retroperitoneal space.
4	Furthermore, extended graft patency can be achieved.
5	
6	Conflict of Interest Statement
7	Masaki Sunagawa and Yukihiro Yokoyama are endowed as chair of the Division of Perioperative
8	Surgery (Yakult Honsha).
9	Figure Legends
10	Fig. 1
11	Axial and coronal computed tomography (CT) scan images of the three patients with large
12	retroperitoneal liposarcomas involving the ipsilateral common iliac artery. The white arrowhead
13	indicates the external iliac artery and the black arrowhead indicates the internal iliac artery. CIA,
14	common iliac artery.
15	
16	Fig. 2
17	Intraoperative photographs (Patient #1)
18	(a) The large retroperitoneal liposarcoma (T) was retracted to the left and the left common iliac artery
19	(Lt-CIA) was taped.

1	(b) The tumor was retracted to the right and the left external iliac artery (Lt-EIA) was taped.
2	(c) Temporal vascular anastomosis between the Lt-CIA and the Lt-EIA was performed using a long-
3	expanded polytetrafluoroethylene (ePTFE) vascular graft to maintain the blood flow in the
4	extremity and secure a clear surgical field (1 st step anastomosis).
5	(d) The surgical field after the <i>en bloc</i> tumor resection. Lt-IIA, stump of the left internal iliac artery.
6	(e) The long <i>in situ</i> ePTFE graft was shortened to a suitable length (2^{nd} step anastomosis).
7	(f) The <i>in situ</i> ePTFE graft was wrapped in the greater omentum to prevent infection of the vascular
8	graft.
9	The dotted white line indicates the edge of the tumor; the solid white line indicates the <i>in situ</i> ePTFE
10	graft.
11	
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Table.1 Clinicopathological features and outcomes of the patients who underwent surgery-the two-step arterial reconstruction technique for resection of the <u>a</u> retroperitoneal liposarcoma with two-step arterial reconstruction technique

	Patient #1	Patient #2	Patient #3
Age	58	77	57
Sex	female	male	male
Comorbidities	none	malnutrition	none
Primary or recurrent	primary	recurrent	primary
Previous operation	none	tumor resection with	none
		colon and kidney	
Diagnosis before surgery	DD-LPS	DD-LPS	DD-LPS
Tumor size (cm)	35×25	18×13	32×21
Location	left	left	left
Combined organ resection	colectomy, nephrectomy	colectomy	colectomy and
	and oophorectomy		nephrectomy
Total operation time (minutes)	790	700	958
Blood loss (ml)	1797	2380	4915
Arterial reconstruction			
Type of graft	7 mm GORE®	10 mm $FUSION^{\mathbb{R}}$	8 mm GORE®
	PROPATEN®		PROPATEN®
1 st step anastomosis			
Length of graft (cm)	70	50	63
Time (minutes)	26	50	39
2 nd step anastomosis			
Length of graft (cm)	13	8	10
Time (minutes)	32	23	25
Time between primary vascular	147	413	290
clumps and final reconstruction			
ICU stays (days)	2	1	3
Postoperative complications	none	surgical site infection	surgical site infection
(Clavien-Dindo grade)		(IIIa)	(IIIb)
Postoperative hospital stays (days)	15	28	63

Pathological diagnosis	WD-LPS	DD-LPS	DD-LPS
FNCLCC grade	1	3	2
Surgical margin	R0	R1	R2*
Recurrence	no	yes	yes
Survival after surgery (days)	252	200	466
Outcome	alive	dead**	alive

ICU, intensive care unit; WD-LPS, well-differentiated liposarcoma; DD-LPS, dedifferentiated liposarcoma; R0, microscopically negative surgical margin; R1, macroscopically negative but microscopically positive surgical margin with well-differentiated component; R2, macroscopical residual tumor

* proton therapy was applied to the remnant tumor

**died with of an other disease

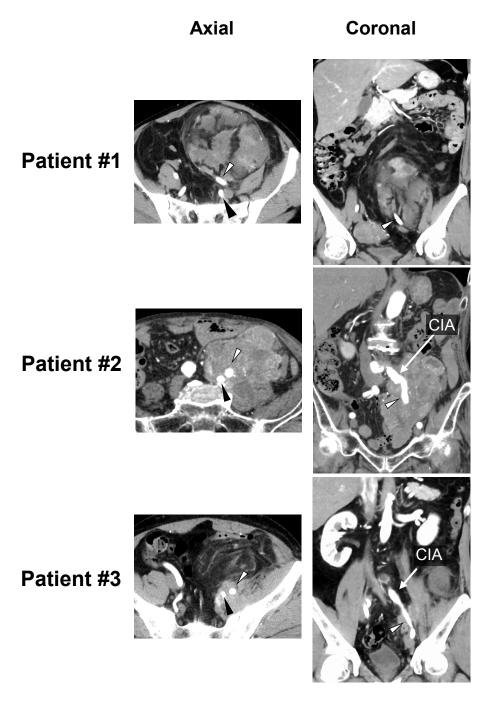


Figure 1