



Oncovascular Surgery: Essential Roles of Vascular Surgeons in Cancer Surgery

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For the modern practice of cancer surgery, the concept of oncovascular surgery (OVS), defined as cancer resection with concurrent ligation or reconstruction of a major vascular structure, can be very important. OVS for advanced cancers requires specialized procedures performed by a specialized multidisciplinary team. Roles of oncovascular surgeons are summarized as: a primary surgeon in vessel-origin tumors, a rescue surgeon treating complications during cancer surgery, and a consultant surgeon as a multidisciplinary team for cancer surgery. Vascular surgeons must show leadership in cancer surgery in cases of complex advanced diseases, such as angiosarcoma, leiomyosarcoma, intravenous leiomyomatosis, retroperitoneal soft tissue sarcoma, iatrogenic injury of the major vessels during cancer surgery, pancreatic cancer with vascular invasion, extremity soft tissue sarcoma, melanoma and others.

Key Words: Oncovascular procedures, Cancer, Vascular surgery, Soft tissue sarcoma

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INTRODUCTION

Surgical resection remains the cornerstone for the curative treatment of malignant tumors. When a tumor mass encases a critical arterial or venous structure, en bloc resection with vascular reconstruction is essential for a successful operative therapy. To ensure successful symptom relief and long-term oncological control, careful preoperative planning within a multi-disciplinary team including oncologists and vascular specialists has critical importance. Although vascular surgeons are frequently involved in cancer surgery, their role is often underestimated and overlooked. Because vascular surgeons are dedicated to treating vascular diseases by medical therapy, endovascular intervention and open surgery, cancer surgery may not be their primary concern. And the primary cancer originating from the blood vessels is quite rare. Therefore, vascular surgeons are usually isolated from many societies for cancer therapy and

seem to be content with the role of a consultant surgeon rather than a primary oncologic surgeon. However, to ensure a safe tumor resection and successful revascularization of certain advanced cancers with vascular involvement, the roles of vascular surgeons are critical. The active participation of a vascular surgeon in cancer therapy can improve oncologic outcomes and patient safety.

In this review, we describe the various roles of vascular surgeons in cancer surgery and encourage all vascular surgeons, especially those in tertiary referral centers, to raise the voice as primary oncologic surgeons for the sake of safety and better outcomes for cancer patients.

TERMINOLOGY OF ONCOVASCULAR SURGERY

The medical term “oncoplastic surgery” is very popular. In the early 1980s, breast cancer resection and simultaneous

breast reconstruction were simultaneously performed, and the concept of oncoplastic surgery has nowadays become widely accepted and practiced [1,2]. The basic concept was treating cancer and preserving the patient's beauty to achieve better aesthetic and quality of life (QOL) outcomes while not compromising oncological effectiveness. For the success of oncoplastic surgery, multidisciplinary therapy is essential.

Oncovascular surgery (OVS) is a similar terminology implying simultaneous oncologic surgery and vascular reconstruction. OVS can be defined as cancer resection with concurrent ligation or reconstruction of a major vascular structure [3]. Oncovascular procedures for advanced cancers are demanding specialized procedures performed by a specialized multidisciplinary team. The procedure requires an extensive understanding of the tumor biology, careful preoperative planning, meticulous vascular surgical techniques, and multidisciplinary collaboration.

Current use of the term "oncovascular surgery" is quite sparse. On a Google search, we found only 3 articles [3-5] and 2 medical centers using this term. A liberal and timely use of this term OVS may increase awareness regarding the important roles of vascular surgeons in complex cancer surgeries among the public and medical professionals.

CONCEPT OF ONCOVASCULAR SURGERY

Complete surgical resection remains the cornerstone of treatment for most malignancies. Traditionally, surgeons have been reluctant to operate on advanced tumors with major vessel involvement due to the inherently increased complexity of these operations and uncertainty about the long-term oncologic benefit. However, several case series reported the feasibility and safety of en bloc vascular resection for extremity sarcoma [6-8], retroperitoneal sarcoma [9,10], or pancreatic cancer [11].

Ghosh et al. [3] published an excellent review article entitled "Oncovascular Surgery". After reviewing multiple electronic health databases, they reported that published outcomes for different malignancies suggest that survival is dependent upon the complete clearance of the primary pathology and tumor biology rather than vascular-related complications. They concluded that major vessel involvement of a tumor mass should not necessarily be considered a barrier to en bloc resection and hence curative surgery. Radical surgical resection may offer the only chance for cure or palliation for these patients.

To ensure the successful surgical resection of these advanced tumors, a multidisciplinary team including oncologic and vascular specialists is essential from the detailed preoperative planning and co-operation to postoperative

management. Vascular surgeons are the best experts to perform major vessel resection and reconstruction. Major vessel injuries induced during cancer surgery can cause serious bleeding and massive transfusion that can jeopardize the patient's life. Vascular surgeons can prevent or minimize these complications by inflow or outflow control and planning of the exact surgical approach through the avascular plane. Early vascular control makes the en bloc resection of the advanced cancer quicker and easier.

VARIOUS ROLES OF VASCULAR SURGEONS DURING CANCER SURGERY

The modern practice of cancer surgery requires the co-operation of vascular surgeons in many ways as primary or consultant surgeons. The role can be classified into three categories: a primary surgeon for vessel-origin tumors, a rescue surgeon for complications during cancer surgery, and a consultant surgeon of a multidisciplinary team for cancer surgery.

1) Primary surgeon for vessel-origin tumors

Primary malignant tumors originating from blood vessels are quite rare but include angiosarcoma from the aorta or peripheral arteries, leiomyosarcoma from the vena cava or peripheral veins, and retroperitoneal sarcoma originating from the retroperitoneal major vessels or encasing major vessels. Intravenous leiomyomatosis (IVLM) is another rare tumor that, although benign, is treated by vascular surgeons.

① Angiosarcoma

Malignant tumors in the aorta can be divided by its origin cell into intimal angiosarcoma, medial leiomyosarcoma, and adventitial fibrosarcoma. Fortunately for patients, these tumors are very rare. Unfortunately for surgeons, these tumors are very difficult to diagnose preoperatively, and most are diagnosed in the advanced stage, resulting in very poor prognosis. Early surgical resection is the mainstay of treatment. Angiosarcoma may mimic an infected aneurysm or mural thrombus [12,13]. It is sometimes diagnosed after open or endovascular repair of abdominal aortic aneurysm (AAA) that presents as an atypical growing mass [14,15]. Clinical suspicion of primary aortic angiosarcoma is most important for early diagnosis and proper surgical treatment, especially in cases of atypical rapid growth of an AAA with a thrombotic mass. We experienced one case of aortic intimal sarcoma mimicking an infected aneurysm that was treated by emergent en bloc resection of the aneurysm and in situ reconstruction (Fig. 1). Unexpectedly,

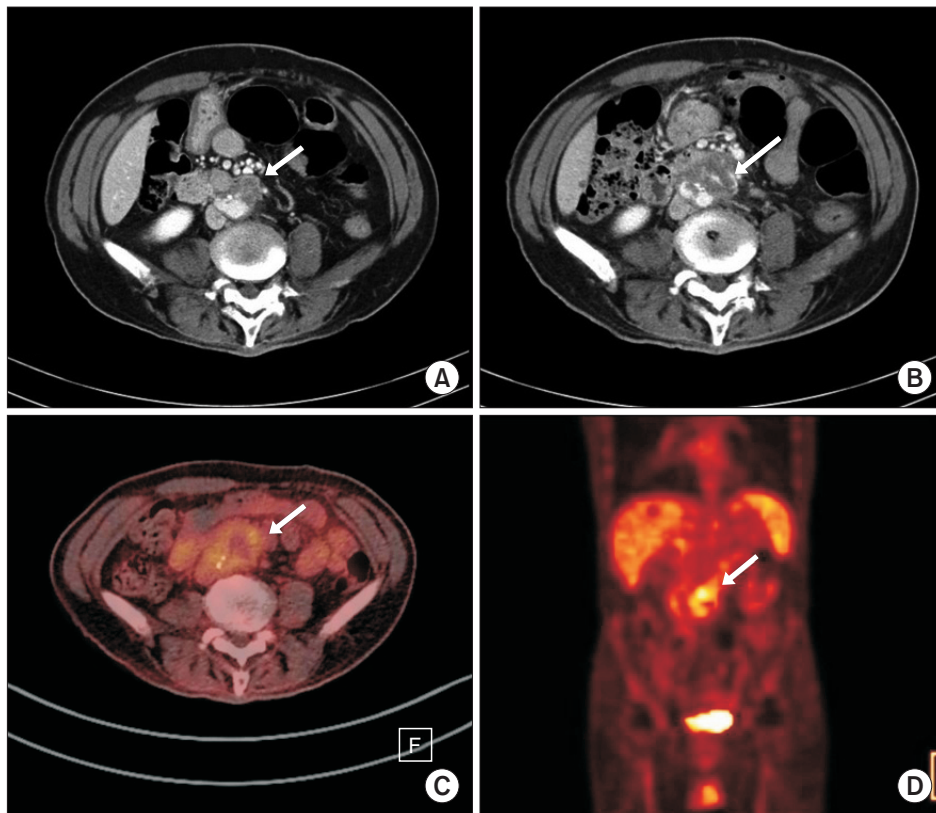


Fig. 1. (A) Initial outside computed tomography revealed a 19×18 mm saccular outpouching lesion of the aorta immediately above the aortic bifurcation (arrow). (B) The lesion increased up to 21×36 mm in 50 days (arrow). (C, D) Positron emission tomography revealed hypermetabolic lesions in the aorta (arrows), bilateral common iliac, and right inguinal area, suggestive of an infected aneurysm and reactive inflammation.

an intimal angiosarcoma was found during the pathologic examination (unpublished data).

② Leiomyosarcoma of the vena cava

Primary tumors of the inferior vena cava (IVC) are rare, and the vast majority (95%) are leiomyosarcoma. Because of its insidious nonspecific symptoms, the diagnosis is often made in the advanced stage and the prognosis is poor. Surgical excision of the tumor and the involved portion of the IVC with negative margins is the only curative treatment, and alternative therapies such as chemotherapy and radiotherapy are ineffective [4,16,17]. Fig. 2 shows a case of late presentation of IVC leiomyosarcoma that originated from infrarenal IVC and grew up to the right atrium. Although the operation is formidable, many surgeons reported improved survival after margin-free resection of the involved IVC portion [4,16,17]. Here we discuss some technical points and debates for this operation.

First, IVC reconstruction after resection can be done in one of three ways: ligation and no reconstruction [18], selective reconstruction [19], or routine reconstruction [10,20]. Daylami et al. [18] reported that IVC reconstruction below the level of the hepatic veins is unnecessary because the slow-growing nature of the tumor permits the development of collateral venous drainage. Graft thrombosis is not infrequent and may risk pulmonary embolism. The policy



Fig. 2. Retroperitoneal leiomyosarcoma arise in the infrarenal inferior vena cava extending up to the right atrium.

of no reconstruction can reduce operation time, prevent pulmonary embolism from lower-extremity deep vein thrombosis, avoid graft-related complications such as graft infection or graft-enteric erosion, and reduce the risk of potential high output cardiac failure and the need for life-long anticoagulation [18]. They found that postoperative

edema is transitory and generally well tolerated if collateral venous drainage was preserved. However, advocates of routine reconstruction insist that retroperitoneal collateral pathways are usually disrupted for complete tumor removal and lower-extremity edema is worsened [20,21].

Second, reconstruction can be done by primary repair, patch repair, or graft interposition. When the expected IVC narrowing is <50%, primary repair can be done; when it is >50%, patch repair can be done. If complete resection of the IVC wall is necessary, graft interposition is performed. As expected, patency is worst after graft interposition. For graft interposition, many conduits have been used, including autologous vein, peritoneum [22], cryopreserved allograft, bovine pericardium, and a Dacron or expanded polytetrafluoroethylene (ePTFE) prosthetic graft. However, the optimal method remains under debate because of the rarity of the disease and reconstruction cases. If bowel resection is required, an autologous vein, especially the internal jugular vein, is preferred to preserve leg veins and reduce the risk of venous complications [20].

Third, the optimal prosthetic graft is yet to be established because of the small sample sizes examined in the literature: ePTFE vs. Dacron; externally supported graft or not; and large (20 mm) vs. small diameter. Quinones-Baldrich et al. [20] prefer to use a smaller diameter (12-14 mm) ringed ePTFE to promote faster velocities through the graft segment, while other studies have used large (>20 mm) externally supported ePTFE [10,21].

Fourth, the role of chemoradiotherapy is usually deferred. Radiation therapy decreases local recurrence but does not improve overall survival for retroperitoneal sarcoma [23,24].

Daylami et al. [18] used neoadjuvant radiation therapy,

followed by curative resection without reconstruction 6 weeks later. Their rationales for preoperative radiation are that dissection is facilitated by radiation-induced edema, and radiation causes IVC wall thickening, giving the vessel an almost arterialized quality and easier handling.

And finally, preservation of the renal and hepatic venous outflow is important. If necessary, the veins can be reconstructed by resection and reimplantation. Liu et al. [25] reported that venoplasty of the renal ostia (VRO) is an effective method for preserving the renal veins and reconstructing renal outflow. In VRO, the ostia of the renal veins are preserved and the IVC–renal vein conjunction can serve as a common end for end-to-end anastomosis with a prosthetic graft. Reconstruction of the left renal vein may be unnecessary due to collateral flow via the gonadal or adrenal vein, but reconstruction of the right renal vein is usually required.

③ Intravenous leiomyomatosis

IVLM is a unique rare benign vascular tumor that originates from the intrauterine venules and grows proximally inside the IVC and reaches the right heart. All affected patients have uterine leiomyoma or a history of hysterectomy. Due to non-occlusive growth inside the vein, most cases are asymptomatic and are sometimes found after extension to the right atrium with cardiac symptoms of syncope, dyspnea, or chest pain. The surgical principles involve removal of the uterine tumor, bilateral oophorectomy, and removal of all intravenous tumors. However, controversy persists about the operation technique of removing advanced tumor from the pelvis to the heart: single-stage vs. two-stage, use of cardiopulmonary bypass (CPB) or not, and median sternotomy and laparotomy vs. laparotomy only.

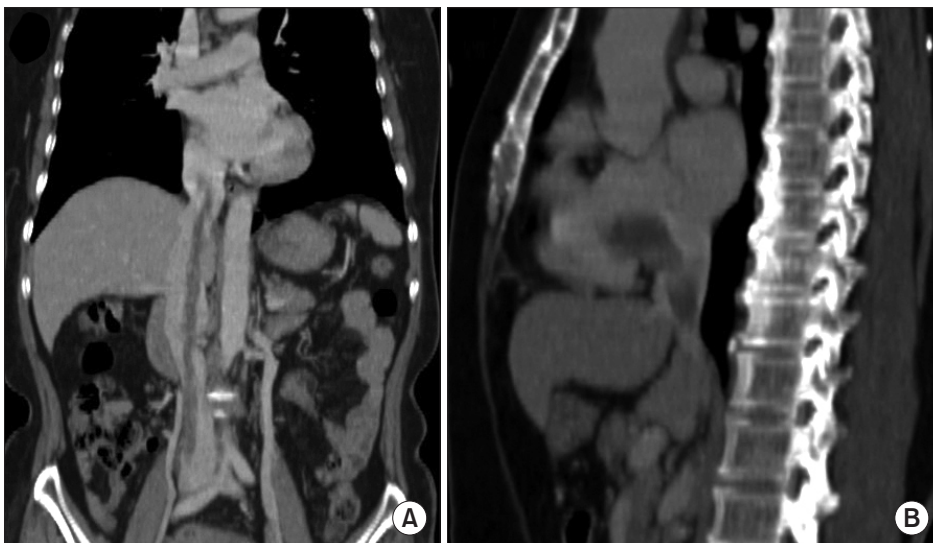


Fig. 3. Computed tomography images of intravenous leiomyomatosis. (A) Tumor is located inside the inferior vena cava, arising from the pelvis and growing proximally with the blood flow. (B) The proximal end of the tumor is located inside the right atrium.

Harris and Karakousis [26] reported successful removal of the tumor using only laparotomy and IVC venotomy. Rispoli et al. [27] reported a single-stage operation via sternotomy with CPB and thoracic tumor excision, followed by a midline abdominal incision and pelvic and IVC tumor removal. They described that the tumor was firm and rubbery without thrombus or an area of friable tissue.

In our experience with several cases, we found that the risk of intraoperative embolization is very unlikely because of the firm and slippery nature of the tumor, which is rarely friable or breakable during removal by traction. An accompanying thrombus in the proximal IVC and atrium is very unlikely because of the non-occlusive growth of the tumor, while distal iliac or femoral thrombus may be associated with the tumor. However, the tumors firmly adhere to the internal iliac vein (IIV) where they originate and enter the systemic circulation, sometimes adhering to the IVC at the ovarian vein confluence. Tumor masses in the IVC or right atrium are usually mobile, with no attachment to the venous wall. Therefore, if we consider the biology of this intraluminal tumor growth, an IVLM extending into the heart can be safely removed in a single-stage operation with an abdominal incision alone. The two-stage operation is usually performed because of a misunderstanding of the disease. Because of the risk of tricuspid incarceration or right heart failure by the tumor, open heart surgery with CPB was usually performed initially, which could only partially remove the tumor near the level of diaphragm. The tumor is usually adherent to the hypogastric vein or the entry site of the IVC; thus, the abdominopelvic approach is sufficient to remove the intracardiac tumor via gentle downward traction. During the operation, we usually monitor the intracardiac tumor using echocardiography in real-time and confirm its floating nature and the lack of residual tumor after removal via downward traction (unpublished data). As shown in Fig. 3 and 4, the tumor is very unlikely to be broken and cause a serious pulmonary embolism.

The operative protocols in our center for IVLM extend-



Fig. 4. Resected specimen of the tumor shows the intracardiac portion on the left and fragmented tumor from the pelvis on the right. The tumor is firm with a glistening surface that is unlikely to cause an embolism.

ing to the right atrium are intraoperative monitoring of the tumor by echocardiography, only laparotomy via a long midline incision, venotomy in the IIV–external iliac vein bifurcation, or common iliac vein confluence. After removal of the distal tumor with the IIV, distal vascular control was achieved by ligation and proximal tumor removal by gentle traction was performed. A blood transfusion should be prepared at this moment. Because clamping of the proximal vein is impossible due to the tumor, significant blood loss can occur. A hysterectomy and bilateral oophorectomy is performed if not performed before. The authors believe that if the cardiac tumor is mobile on echocardiography, sternotomy and CPB is unnecessary.

④ Retroperitoneal soft-tissue sarcoma encasing major vessels

Retroperitoneal soft-tissue sarcomas (RSTSs) are rare and often difficult to manage because of the extensive nature of the tumor. The role of vascular surgeons is especially important in such cases of troublesome malignancies. Surgical resection is the cornerstone of treatment, and the capacity to achieve an R0 resection during the primary resection attempt is essential for any chance of potential cure or long-term survival. The standard treatment of these lesions is compartmental resection and en bloc resection of the tumor mass and of the adjacent organs and tissues [5]. Bertrand et al. [4] reported oncovascular compartmental resection for RSTS with vascular involvement. OVS was performed in 126 patients, including liposarcoma (55%) by the vascular/oncology team, and it was concluded that vascular resection and reconstruction are safe and feasible for RSTS. The morbidity rate was acceptable, with no perioperative deaths. Despite high recurrence rates, oncovascular resection enhances resection margins and allows encouraging survival results for patients with otherwise unresectable diseases.

RSTS involving major blood vessels may arise from the blood vessels or advanced stage of other sarcoma in contact with the vessel or encasing it. In such patients, compartmental resection including resection of the major blood vessels and reconstruction must be discussed preoperatively, and vascular surgeons are the best specialists to decide the surgical approach, resectability, reconstruction method, and conduit. The vascular surgical technique can minimize inadvertent major vessel injury and massive bleeding. The early resection of major blood vessels may ease the tumor resection and reduce bleeding and operative time. Therefore, active involvement of vascular surgeons in the treatment of RSTS as a primary surgeon is warranted, especially in tertiary referral centers. Fig. 5 shows a rare case of follicular dendritic cell sarcoma abutting the portal vein (PV)

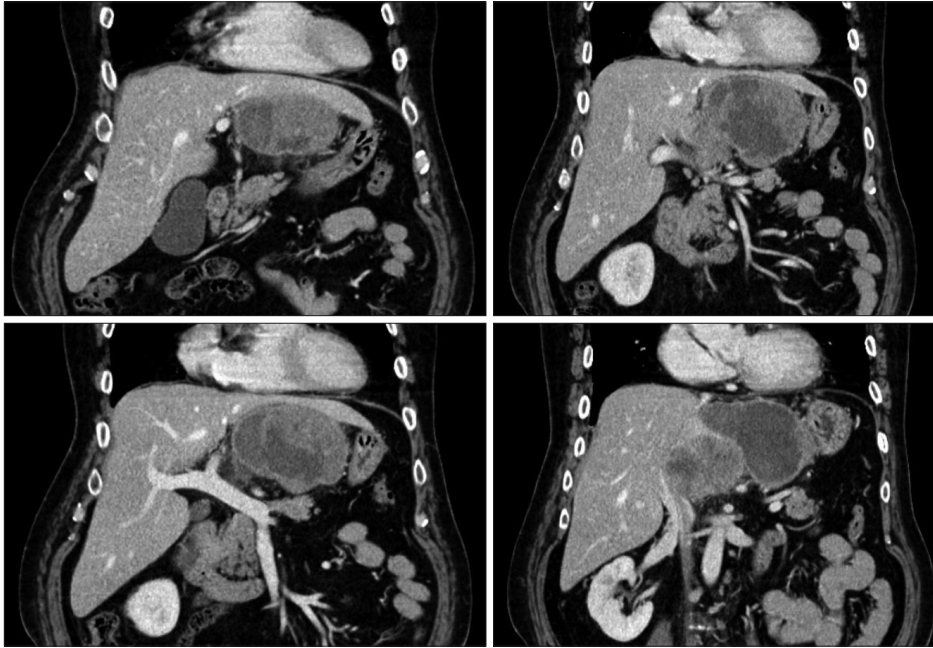


Fig. 5. Preoperative computed tomography suggests the tumor abutting on the portal vein and vena cava. Pathology resulted in a follicular dendritic cell sarcoma without invasion.

and vena cava. Because the preoperative images highly suggest the need for major vessel resection and reconstruction, a vascular surgeon operated this case, and the tumor was completely removed without vessel resection.

Luu et al. [28] reported an interesting idea that two-stage RSTS (femoro-femoral bypass preceding resection) can reduce oncologic resection time and postoperative intensive care unit stays. Two or four weeks after femoral bypass, the tumor was resected en bloc with the involved arterial venous branches without in situ reconstruction. Although they failed to prove better oncologic outcomes or less bleeding, this approach can be used in extensive RSTS involving the iliac vessels.

2) Rescue surgeon treating complications during cancer surgery

Many emergent calls for vascular surgeons during operations occur in tertiary referral centers, and the cause of the call can be categorized as follows: iatrogenic injury with bleeding, acute thrombosis of the artery due to dissection or plaque rupture, acute thrombosis of the vein, vascular invasion and need for reconstruction, vascular exposure, and endovascular adjunctive therapy.

Manzur et al. [29] reported that vascular surgery is an essential hospital resource in modern health care, that emergency intraoperative calls for vascular surgeons are common, and that 56% of the consultations are unplanned. The most common cause of emergent consult was bleeding (33%), followed by need for vascular reconstruction, limb

ischemia, and vascular exposure. The consultations were done by every surgical specialty, most commonly by urology, hepatobiliary/transplant, and cardiac surgery. In modern tertiary referral centers, the cause of vascular trauma is usually iatrogenic. Intraoperative or immediate postoperative calls for vascular surgeons are common after oncologic surgery or interventions. Vascular surgeons should be aware of the mechanism of vascular injury during orthopedic, urologic, and laparoscopic surgeries. The presentations of vascular injury are diverse, including active bleeding by transection or laceration of the vessels, dissection, false aneurysms with delayed rupture, arteriovenous fistulas, acute thrombosis, and contusion with late thrombosis. To cope with the various types of vascular injury, vascular surgeons should train every oncologic surgeon regarding the basic vascular surgical technique. There are several ways of hands-on training of surgical skills for surgical residents and fellows, including lectures, dry and wet lab, and cadaveric dissection. After learning the basic vascular techniques, oncologic surgeons can repair the vessel injury by themselves or are less likely to injure the vessels by crude handling with traumatic instruments or clips.

3) Consultant surgeon as a multidisciplinary team for cancer surgery

Locally advanced tumors encasing or invading adjacent major vessels require cooperation of the oncovascular surgeon as a multidisciplinary team member. There are many examples of OVS consult operations.

① General surgery

OVS is often required in pancreatic cancers invading the PV or hepatic artery (HA), rectal cancers invading the iliac vessels, thyroid cancers with internal jugular vein or carotid invasion, and adrenal tumors encasing renal vessels. One of the most common examples of OVS is cancer invasion to the major vessels by pancreatic cancer. In our tertiary referral center, we have a well-organized multidisciplinary team including a pancreatic surgeon, a vascular surgeon, and an interventional radiologist and oncologist [30]. When invasion of the PV or HA is suspected on preoperative computed tomography or magnetic resonance imaging, we make a preoperative plan together, and the pancreatic surgeon performs the resection. If definite vascular invasion is observed intraoperatively, the vascular surgeon resects the involved PV/HA en bloc with the tumor and immediately reconstructs the vessel to minimize bowel edema or liver ischemia. Various vascular surgical techniques are used as a patient-tailored surgery (Fig. 6): primary end-to-end anastomosis of the PV, primary repair with a bovine patch, interposition graft with a short tubular graft made of a bovine patch, and interposition graft with a spiral graft made of saphenous vein [31]. We usually avoid using a prosthetic graft because of the risk of infection.

Sgroi et al. [11] reported that vascular reconstruction plays an important role in the treatment of pancreatic adenocarcinomas. They concluded that pancreaticoduodenectomy with vascular reconstruction is a reasonable approach for T3N0 and T3N1 pancreatic adenocarcinoma invading

the PV or HA (1-year survival rate, 71.1%), and an aggressive surgical approach can improve survival in high-volume institution.

② Orthopedic surgery for extremity soft-tissue sarcoma

Extremity soft-tissue sarcoma (ESTS) invading the femoral or brachial vessels presents major challenges to surgeons because of the risk of amputation, frequent recurrence, and poor long-term survival. When ESTS invades the major vessels, amputation was previously considered for complete oncologic resection because of the high recurrence rate and hematogenous metastasis after local resection. However, limb salvage surgery with vascular reconstruction is currently considered the standard treatment for ESTS because surgical resection with adequately wide margins showed equivalent oncologic results and significantly better QOL than amputation [32]. To ensure better oncologic control, it is recommended that whenever it is impossible to achieve a wide resection margin without vascular resection, active vascular resection be indicated [33–35]. There is a critical role of vascular surgeons in the curative surgery for ESTS. Schwarzbach et al. [36] reported the results of their study on 21 patients who underwent vascular resection for lower-limb ESTS. At a median follow-up of 34 months, the primary and secondary patency rates of arterial (venous) reconstructions were 58.3% (54.9%) and 78.3% (54.9%), respectively. The limb salvage rate was 94%, and 5-year survival rate was 52%.

We previously reported the outcomes after arterial or

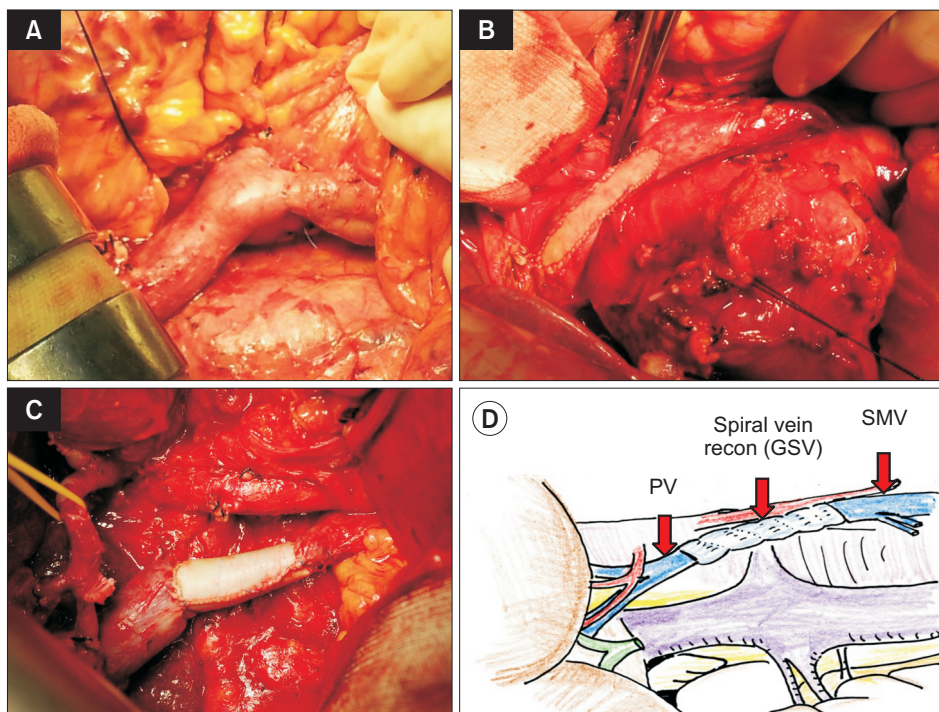


Fig. 6. Various reconstruction of the portomesenteric vein after en bloc resection of pancreatic cancer. (A) Primary end-to-end anastomosis of the portal vein (PV), (B) primary repair with a bovine patch, (C) interposition graft with a short tubular graft made of a bovine patch, and (D) an interposition graft with a spiral graft made of saphenous vein. GSV, great saphenous vein; SMV, superior mesenteric vein.

venous reconstructions in limb salvage surgery for ESTS [35]. The autologous vein conduit showed better 2-year graft patency than that with the prosthetic graft (83.3% vs. 14.3%, $P < 0.001$), and venous reconstruction showed more occlusions than arterial reconstruction, although the difference was insignificant (38.5% vs. 21.4%, $P = 0.37$). After a median follow-up of 23.3 months, the local recurrence rate was 47% and overall limb salvage rate was 88%, and most of the patients (87%) were ambulatory without assistance devices. We usually try to reconstruct both the artery and vein after en bloc resection if the quality of the contralateral autologous vein conduit is good. However, if a prosthetic graft is to be used, vein reconstruction is not mandatory. We believe that limb salvage surgery of ESTS combined with vascular reconstruction results favorable functional outcome with comparable survival outcomes despite high local recurrence rates.

③ Inguinal or popliteal node dissection in melanoma

The current standard of care for melanoma of intermediate thickness (Breslow depth, 1.0–4.4 mm) is wide excision and sentinel node biopsy [37,38]. If the sentinel node is positive for malignant cells, then complete lymph node dissection is performed. Often, for inguinal or pelvic metastasis, iliac or pelvic node dissection is performed. Vascular surgeons are so familiar with the inguinal and iliac vessel anatomy that they can easily perform complete node dissection without vessel injury or residual node metastasis.

CONCLUSION

In the modern practice of cancer surgery, the concept of OVS, which can be defined as cancer resection with concurrent ligation or the reconstruction of a major vascular structure, can be very important. Oncovascular procedures for advanced cancers require specialized procedures performed by a specialized multidisciplinary team. The roles of oncovascular surgeons are summarized as a primary surgeon in vessel-origin tumors, a rescue surgeon treating complications during cancer surgery, and a consultant surgeon as a multidisciplinary team for cancer surgery. Vascular surgeons must show leadership in cancer surgery for in cases of complex advanced disease including angiosarcoma, leiomyosarcoma, IVLM, RSTS, iatrogenic injury of the major vessels during cancer surgery, pancreatic cancer with vascular invasion, ESTS, melanoma, and others.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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