

Prosthetic replacement of the inferior vena cava for malignancy

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Purpose: Invasion of the inferior vena cava (IVC) by tumor is generally considered a criterion of unresectability. This study was designed to review the outcomes of a strategy of aggressive resection of the vena cava to achieve complete tumor resection coupled with prosthetic graft placement to re-establish caval flow.

Methods: Retrospective review of patients treated at a university referral center. Ten patients (mean age 54; eight females, two males) underwent tumor resection that involved circumferential resection of the IVC and immediate prosthetic replacement with ringed polytetrafluoroethylene (PTFE) grafts ranging in diameter from 12 to 16 mm.

Results: Seven patients had replacement of the infrarenal IVC, two of their suprarenal IVC, and one had reconstruction of the IVC bifurcation. Four of the 10 patients received preoperative chemotherapy, and none received radiotherapy. The most common (7/10) pathologic diagnosis was leiomyosarcoma arising from the IVC or retroperitoneum. Additional diagnoses included teratoma (one), renal cell carcinoma (one), and adrenal lymphoma (one). There were no perioperative deaths, and one complication (prolonged ileus) occurred. Mean length of stay was 8.1 days. Anticoagulation was not routinely used intraoperatively or postoperatively. Follow-up (mean duration = 19 months) demonstrated that survival was 80% (8/10) and 88% (7/8) of patients were free of venous obstructive symptoms.

Conclusion: Resection of the IVC with prosthetic reconstruction allows for complete tumor resection and provides durable relief from symptoms of venous obstruction. (J Vasc Surg 1998;28:75-83.)

Involvement of the vena cava by retroperitoneal malignancy is generally indicative of advanced disease and is often considered a contraindication to attempted resection. The ability of non-surgical therapy to cure or palliate these tumors is variable and dependent on the tumor type, but generally in the absence of surgical resection, patient survival is limited.¹ Tumors originating in the kidney, adrenal gland, soft tissues of the retroperitoneum as well as the liver may invade the inferior vena cava and have a dismal prognosis regardless of tumor type if resection is not possible.¹⁻³

Caval involvement has traditionally been suspected by the presenting symptoms of lower extremity swelling and venous engorgement.^{1, 4} The widespread use of preoperative computerized tomography scans has demonstrated that many asymptomatic patients have involvement of the vena cava by tumor, and venograms in these patients have demonstrated extensive venous collaterals that reconstitute the vena cava above the level of obstruction by tumor.⁵ Although these patients may not manifest symptoms of their caval obstruction preoperatively because of adequate collateral flow, resection of the tumor often disrupts the retroperitoneal collaterals. If the removal of the tumor includes caval resection and ligation, then venous drainage through both the collaterals as well as the cava is lost. Thus patients who were asymptomatic before resection have been reported to manifest symptoms of venous obstruction in the lower extremities postoperatively.¹

Recent reports have centered on the use of various techniques to aid in the achievement of complete tumor resection.^{2, 5} These include preoperative

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chemotherapy, either alone or in conjunction with radiotherapy, to attempt shrinkage of tumors. Postoperative radiation therapy can theoretically aid in local control of residual microscopic disease, although many soft-tissue sarcomas are relatively radioresistant. Caval resection and reconstruction techniques, including patch reconstruction with either prosthetic material or autogenous vein as well as replacement of entire segments of the cava with prosthetic tube grafts, have been described as allowing successful complete extirpation of otherwise unresectable tumors.^{2, 3}

However, the examination of patients after modern resection techniques of the inferior vena cava has been limited. Aside from individual case reports, the two large clinical series reported to date^{2, 3} both involve inferior vena caval resection and replacement as an adjunct to major liver resection in the majority (75%) of patients and have outcome data that is limited by short follow-up (mean follow-up periods of 8.8 months² and 15 months³). Experience with this type of operation at an individual institution remains very limited, with the two largest series having only eight and four patients, respectively.^{2, 3}

The purpose of this study was to determine the outcomes of our experience with prosthetic replacement of the vena cava for retroperitoneal malignancies. Our experience reflects that of a tertiary referral center for complex oncology patients in a number of surgical disciplines, and thus a variety of tumors were encountered, similar to that of previous reports of regional referral centers.² The focus was on the long-term outcome of replacement of the inferior vena cava with a prosthetic tube graft, unlike other studies that include reconstructions of both the superior and inferior vena cava with a variety of materials.²⁻⁴ Consequently, we specifically excluded patients with similar tumors who underwent caval resections involving reconstruction with either a prosthetic patch or autologous materials.

METHODS

A review of all available medical records at UCLA Medical Center identified 19 patients who underwent vena caval surgery as a part of an oncologic resection. Of these, nine had either a prosthetic patch repair of the cava, an autologous patch reconstruction, or simple ligation. These patients were consequently excluded from this review, leaving 10 patients who underwent replacement of a segment of the inferior vena cava with a prosthetic tube graft. These patients were treated in a four-year

period (1993-1997). There were eight females and two males, with a mean age of 54.1 years and an age range of 36 to 72 years.

Medical records were reviewed and pertinent data regarding presenting symptoms, diagnostic evaluation, surgery, and postoperative course were extracted. Follow-up was conducted by outpatient examination or telephone, and symptoms were classified according to the updated reporting standards of the Society for Vascular Surgery (SVS) and the North American Chapter of the International Society for Cardiovascular Surgery (ISCVS).⁶ Functional status of the patients was determined according to the Performance Status classification of the Eastern Cooperative Oncology Group (ECOG).⁷ Repeat duplex studies were attempted in every patient at the time of this review; however, the wide geographic distribution of these referral patients made access to these follow-up studies difficult for most patients.

RESULTS

Preoperative evaluation

All patients underwent preoperative CT scanning of the abdomen and pelvis with intravenous and oral contrast (Fig. 1A). Venograms were performed in three of 10 patients by referring physicians (Fig. 1B), but were not routinely done preoperatively. Two of these demonstrated caval occlusion, and one showed significant narrowing. Tumor histology included leiomyosarcoma arising from the IVC or retroperitoneum in seven patients, teratoma (one), renal cell carcinoma (one), and adrenal lymphoma (one). Four patients (three with leiomyosarcoma, one with teratoma) were treated with preoperative chemotherapy; none received preoperative radiation therapy. No patient had symptoms of venous obstruction.

Surgery

All patients were explored through an anterior abdominal incision. Mean estimated blood loss was 1789 ml (range 500-4000 ml), and an average of 2 units of red blood cells (range 0-7 units) were transfused intraoperatively. Ringed PTFE grafts were used in all patients, and diameters ranged from 12 mm for an iliac vein to 16 mm for an IVC graft. The most common (7/10, 70%) graft size was 14 mm. Seven patients had replacement of the infrarenal IVC (Fig. 1C), two of their suprarenal IVC, and one had reconstruction of the IVC bifurcation. No patient underwent replacement of the retrohepatic IVC, and hepatic vascular exclusion was not

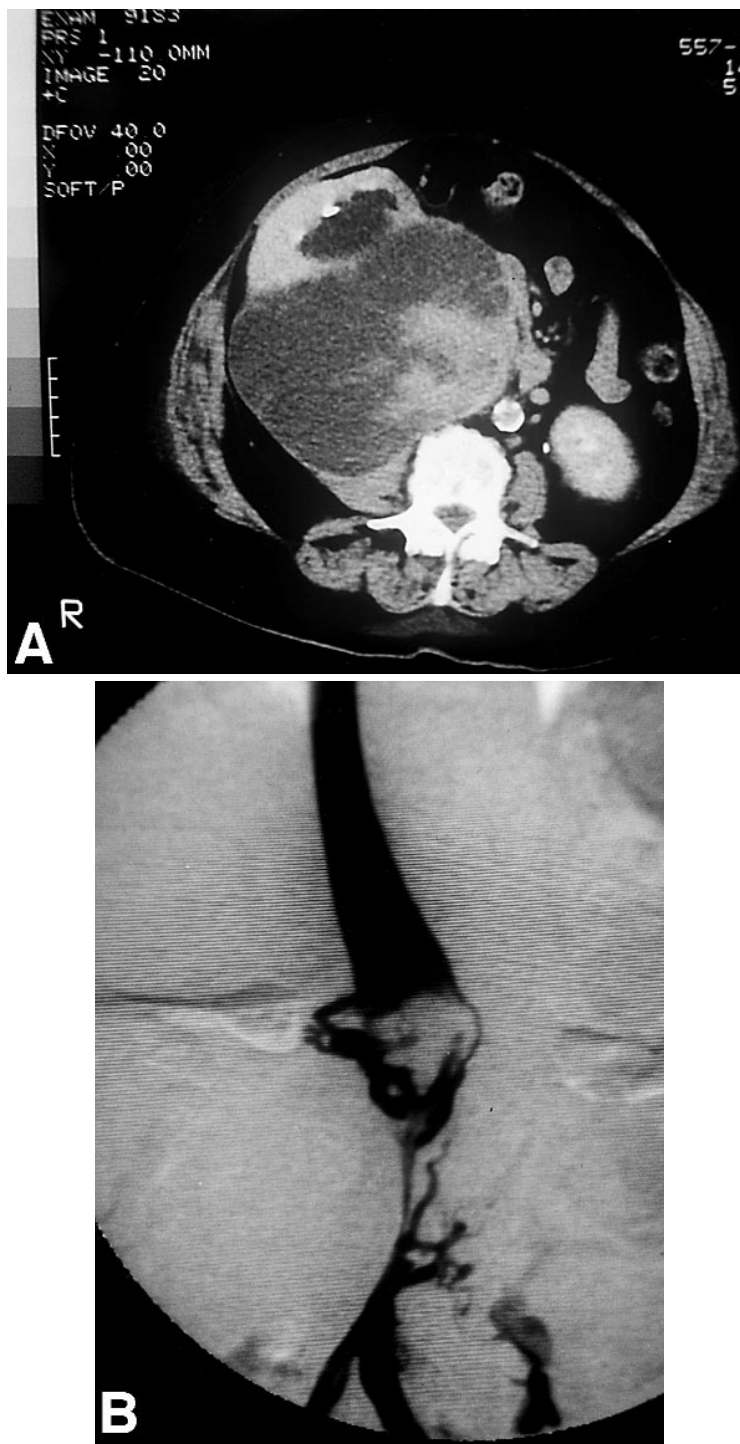


Fig. 1. A, Preoperative computerized tomography, showing large retroperitoneal tumor with vena cava involvement. B, Preoperative venogram, showing tumor invasion of the perirenal vena cava.

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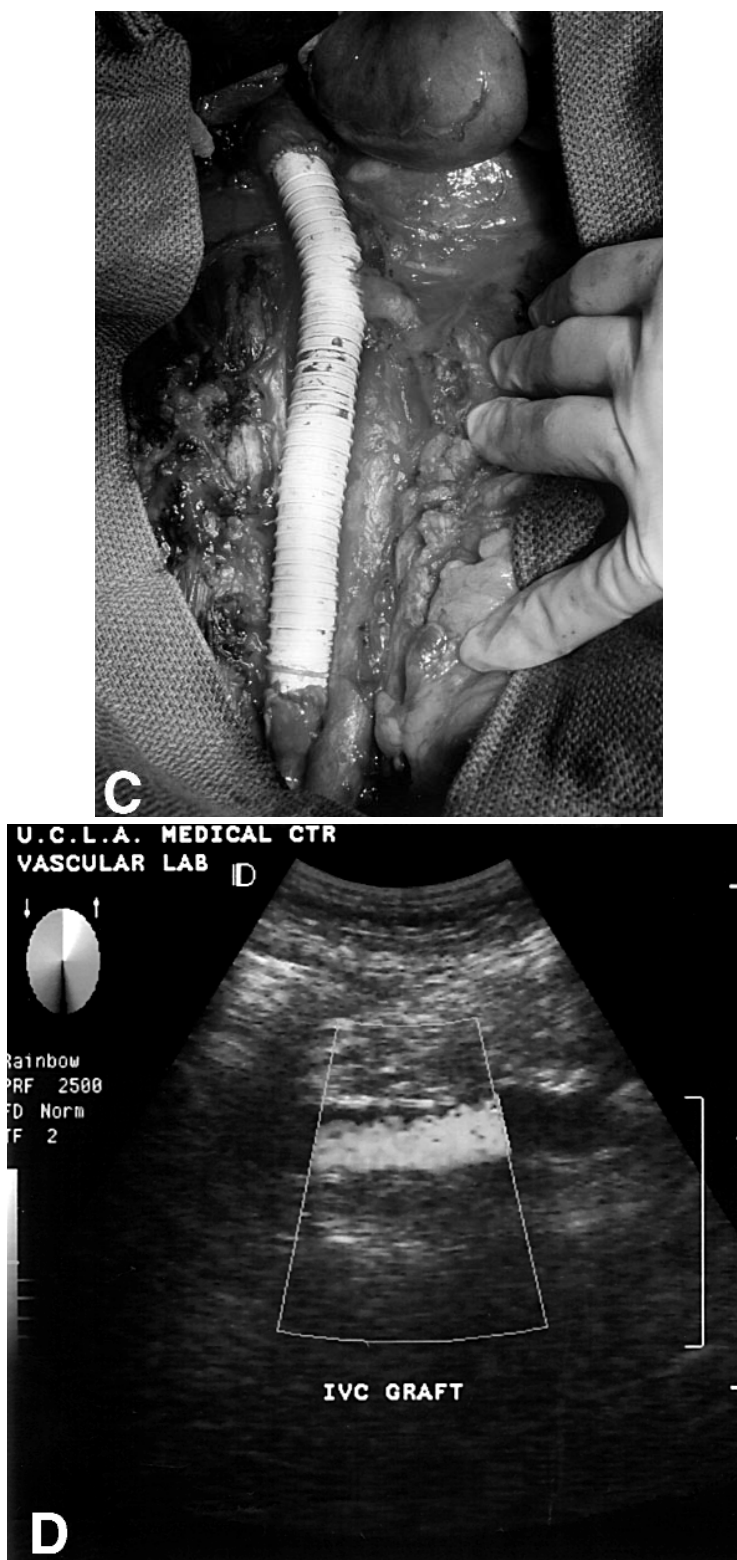


Fig. 1. Cont'd C, Resection required removal of the right kidney in conjunction with the suprarenal and infrarenal vena cava, and prosthetic replacement and reimplantation of the left renal vein into graft. Note preservation of rings in the area of implantation of the left renal vein. Graft chosen to be smaller than proximal and distal remaining cava. **D,** Follow-up duplex scan on patient with inferior vena cava replacement, showing patency of the graft.

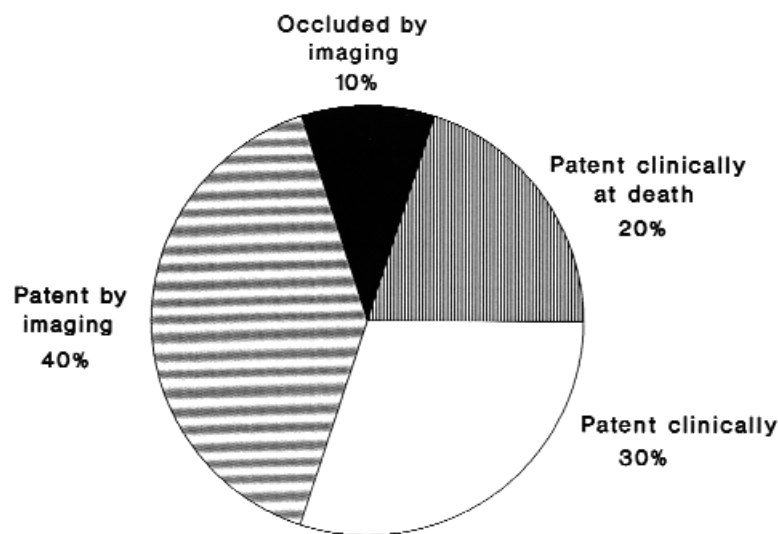


Fig. 2. Graph illustrating status of IVC grafts at follow-up.

required in any patient. An adjunctive groin arteriovenous fistula² to increase flow through the graft was not used in any patient. Intra-operative heparin was used in only one patient, who had both renal veins clamped and then sequentially reimplanted into the prosthetic graft.

There were no perioperative deaths, and the mean duration of hospital stay was 8.1 days. There were no re-operations. Negative tumor margins were obtained in all patients. One postoperative complication occurred, consisting of prolonged ileus that resolved without additional intervention. Pulsatile compression boots and graduated pressure stockings were used in all patients. Anticoagulation was not used postoperatively. There were no postoperative episodes consistent with venous obstruction, and CT scans or duplex studies obtained in six of the 10 patients before discharge demonstrated patency of the IVC graft in all six.

Follow-up

The mean duration of follow-up was 19 months. There were eight survivors and two deaths because of recurrent disease. The average time to death was 14 months, and the average time of survival is 21 months. This average survival represents a disproportionate number of operations performed within the past year (4/7); the other three survivors have all lived longer than three years.

Patency of the IVC grafts was assessed by either imaging studies or clinical follow-up. The patency of five of the eight grafts has been confirmed by

either duplex scan (Fig. 1D) or contrast-enhanced CT scan (mean follow-up 16 months). A graft was defined as being clinically functional if there were no signs or symptoms of venous obstruction, recognizing that the latter may occur in spite of an occluded graft. The basis for this definition includes the finding that ligation of an occluded IVC without reconstruction results in clinical venous obstruction,¹ because of concomitant ligation or resection of collateral pathways. This is further supported by the immediate onset of venous obstructive symptoms in the single patient with late postoperative graft occlusion. This patient had a graft known to be patent by duplex at the time of discharge that occluded 10 months later during a prolonged period of immobilization and hypovolemia secondary to chemotherapy-induced neutropenic sepsis. The patient is currently on oral anticoagulation. Both patients who died had clinically functional grafts at the time of death. Autopsies were not performed. The mean follow-up in the three remaining grafts defined as clinically functional was 21 months. Overall, 90% (9/10) of grafts were patent or clinically functional at follow-up (Fig. 2), and 88% (7/8) of surviving patients were free of venous symptoms.

The functional status of the surviving patients is good, with six able to undertake strenuous activity without limitations (ECOG Performance Status 0). The two remaining patients live independently and ambulate with some assistance (ECOG Performance Status 2). Only one patient, with graft occlusion sec-

Table I. Patient data.

<i>Patient number</i>	<i>Age/Gender</i>	<i>Tumor type</i>	<i>Caval segment</i>	<i>Follow-up (months)</i>	<i>Status/Symptoms</i>	<i>Patency assessment</i>
1	56/F	Leiomyosarcoma	Infrarenal	10	Lower extremity edema	Duplex (occluded)
2	58/M	Leiomyosarcoma	Perirenal	7	No symptoms	Clinically functional
3	69/F	Renal cell	Suprarenal	8	No symptoms	CT scan
4	72/F	Leiomyosarcoma	Entire IVC	18	Died 18 months	Clinically functional
5	41/F	Leiomyosarcoma	Infrarenal	9	Died 9 months	Clinically functional
6	43/F	Leiomyosarcoma	Infrarenal	48	No symptoms	Clinically functional
7	55/F	Adrenal lymphoma	Infrarenal	32	No symptoms	CT scan
8	66/F	Leiomyosarcoma	Infrarenal	32	No symptoms	Duplex
9	45/M	Teratoma	Iliac + infrarenal	7	No symptoms	Clinically functional
10	45/F	Leiomyosarcoma	Infrarenal	19	No symptoms	CT scan

ondary to neutropenic sepsis, is taking long-term oral anticoagulation. Using the SVS/ISCVS reporting standards for venous disease⁶, this patient has Class 3 venous changes (edema without skin changes); another patient has Class 2 disease (varicose veins), and the other six surviving patients have Class 0 (none) disease.

DISCUSSION

The findings in our study of prosthetic replacement of the IVC for the treatment of malignancy support the view that caval replacement can be done safely with good long-term functional results.² This report of 10 patients represents the largest series in the literature to date of patients with prosthetic replacement of the IVC. The survival after aggressive resection of these tumors is measured in years, and our study confirms this with double the follow-up period (19 vs. nine months) of the other long-term series in the literature.² The ability to safely accomplish caval resection without perioperative death and the excellent functional results in terms of patient activity are also noted in our series.

However, there are several significant differences between our study and the two series previously reported.^{2, 3} In the majority of patients (75%) undergoing graft replacement of the cava in both prior studies, concurrent major liver resection was performed. In contrast, none of the patients in this study had concurrent major liver resection because the tumors primarily originated from the cava itself or the adjacent kidney or adrenal. In the prior-reported series the most common tumors were primary or metastatic tumors arising in the liver, and consequently 75% of those cases involved resection and replacement of the retrohepatic IVC. Although our patients had tumors originating from a variety of retroperitoneal organs (Table 1), they all had resection and replacement of various segments of the

intrahepatic IVC. Thus our experience is more reflective of malignancy arising in or around the cava, rather than a caval resection as an adjunctive maneuver to aid in an extended hepatectomy. Not surprisingly, the operative incision and blood loss are also very different in our series from other reports in which IVC replacement accompanied major hepatic resection.² When hepatic resection was involved, a thoracoabdominal incision was routinely used, and the transfusion requirement was more than twice that of our experience.² This difference is also illustrated by the lack of use of hepatic vascular exclusion in our series, as compared with the two prior series, in which 77% of patients required this maneuver and 44% required veno-venous pump bypass.^{2, 3}

The use of ring-reinforced PTFE is common for replacement of the IVC.^{2, 3} The ring-reinforcement in theory resists respiratory compression better, and thus prevents graft collapse that may be a factor in promotion of thrombosis. Experimental studies confirm the ability of ring-reinforcement to prevent hemodynamic changes associated with graft deformation.⁸ A comparative study with non-ringed grafts has not been done and is not feasible given the small numbers of patients in even the largest reports with this technique. We generally favor placement of a graft smaller than the surrounding native cava, as this promotes a higher blood velocity through the graft and thus may minimize blood-prosthetic interactions that promote thrombus formation. We did not use groin arteriovenous fistula to increase IVC blood flow as others have reported.²

Routine anticoagulation was not used either intraoperatively or postoperatively, and the good long-term patencies achieved using this strategy in our series make us question the suggestion that life-long oral anticoagulation is required with prosthetic replacement of the IVC.² The one episode of graft thrombosis in our experience occurred in a patient

who subsequently became critically ill and hypovolemic 10 months after caval replacement. This experience, although quite anecdotal, suggests that short-term anticoagulation should be instituted when a known risk factor for venous thrombosis (e.g., immobilization, dehydration, or subsequent major surgery) develops in a patient with a prior IVC prosthetic graft.

Despite the majority of patients (7/10, 70%) in our series who had a leiomyosarcoma of the IVC, no patient had symptoms or signs of venous obstruction. This is consistent with other large reviews of IVC leiomyosarcoma, which note that only 20% to 30% of patients have venous symptoms, presumably because of the development of large retroperitoneal collaterals.^{1, 5, 9} The argument has been made that replacement of the IVC with prosthetic material is unnecessary in asymptomatic patients and even in patients with venous symptoms.^{1, 9}

Long-term survival in patients with leiomyosarcoma of the IVC is dependent on radical resection, and neither chemotherapy nor radiation therapy have increased long-term survival.^{1, 5} Survival after complete resection of leiomyosarcoma of the IVC is significantly greater than sarcomas of either the aorta or pulmonary artery.¹⁰ The ability of caval resection to contribute to successful radical resection is illustrated by the finding that negative tumor margins were achieved in every patient in our series.

Our indications for replacement of asymptomatic occluded cava include any situation in which the retroperitoneal dissection or resection has removed the pre-existing collaterals. This is often the case in oncologic resection. We would not recommend caval replacement if there is hemodynamic instability or bilateral iliac occlusion that would make re-establishment of venous continuity within the abdomen impossible or hazardous. Our series includes one patient who had an iliac to suprarenal IVC graft for a pelvic teratoma (Table 1, Patient #9).

The limitations of the present study include the relatively short mean follow-up period and the lack of follow-up duplex studies in all patients. The use of CT scan for follow-up gives an overall image of contrast flow through the graft, but may miss smaller areas of thrombus deposition that theoretically could either embolize or predispose to graft thrombosis. An average follow-up of 19 months does not mean that late graft occlusion will not subsequently occur, and there is the small possibility that a patient may have an asymptomatic graft occlusion, as has been described only once before in the literature.¹¹ The one patient in our study who had both clinical

and duplex evidence of sudden graft occlusion is the only patient described with clinical evidence of graft occlusion. Thus there appears to be good correlation between symptoms and graft occlusion after surgical resection of the collaterals, in contrast to the preoperative state, during which gradual occlusion is often tolerated because of development of retroperitoneal collaterals.

Radical resection of a retroperitoneal tumor often disrupts collateral venous channels, and the use of simple ligation of the IVC is associated with postoperative venous symptoms that have required long-term anticoagulation.¹ In contrast, our results demonstrate that prosthetic IVC replacement can be safely accomplished without intraoperative or postoperative anticoagulation and that function of both grafts and patients is good.

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DISCUSSION

Dr. Robert C. Lim, Jr. (San Francisco, Calif.). The goal of cancer surgery is to resect for cure, which requires resecting all visible and microscopic tumors. For tumors that invade the inferior vena cava (IVC), the principle is no different. This paper restates that the IVC can be resected and replaced with a graft. I commend the authors for bringing this to our attention. In cancer of the IVC, the tumor either arises from the IVC, as in leiomyosarcoma, extends into the IVC, as in renal cell carcinoma, or invades into the IVC, as in adrenal cell carcinoma.

Most of the time, IVC obstruction by tumor is slow, and collateral flow develops, which might make en bloc resection possible without canal reconstruction. The morbidity rates from venous hypertension in these cases are minimal. This paper draws our attention to the small percentage of cases when venous hypertension is unacceptable and a graft is necessary.

Again, the goal of resection of the cancer is en bloc resection; reconstruction is next. Simple ligation of the IVC can be done in the infrarenal segment. If involvement is extensive, reconstruction with a graft may be necessary as described by the authors. I wish to submit a third method, which is primary end-to-end anastomosis. To bridge a small gap, ligation and division of a number of lumbar veins above and below the gap plus ligation and division of the hypogastric veins to mobilize the iliac veins, as in renal transplantation, will allow the entire venous system to give you a segment of vein for a tension-free anastomosis.

This leads to my first question to the authors. Can you give information on the length of the IVC involved in the resection leading to the use of a graft?

In the manuscript, the authors used the term "clinically patent." What does this mean? Does this mean no leg edema or swelling? Vascular surgeons in the late 1960s and early 1970s performed a large number of emergency venous thrombectomies for acute iliofemoral thrombophlebitis. The immediate results were dramatic; the swelling decreased and the pain disappeared. All patients were "clinically improved." Dr. Karp and the late Dr. Wylie studied a group of these patients and reported a high thrombosis rate in spite of good clinical outcome. Therefore, I would be careful in reporting patency without hard data.

The mean survival of patients with IVC cancer has been reported at about 40 months. The prognosis is poor in these patients. In the group of surviving patients presented, half were in the last year and three were in the last 3 years of the 4-year study. I do not believe that we have had a good long-term result yet. The long-term function of graft and patient is not known clearly at this time. I did not see any follow-up abdominal computed tomography data on these patients in the manuscript. Would the authors share this if they have it?

In closing, I can agree with the first part of the authors' conclusion "that resection of the IVC with prosthetic reconstruction safely allows for complete tumor resection." However, I am not convinced on their statement that "it provides durable relief from symptoms of venous obstruction." The sequel of chronic venous hypertension often takes years to develop.

Dr. William J. Quinones-Baldrich. Thank you, Dr. Lim, for your comments and the review of our manuscript.

We specifically eliminated from inclusion in this study patients who underwent primary repair of the vena cava where either a primary end-to-end anastomosis or some type of patch reconstruction, either autogenous or prosthetic, was used to close the gap created by the resection. So, these are all cases where the entire vena cava was replaced with a prosthetic graft.

Your first question asked how much length of vena cava above and below the graft is necessary for a complete resection. This was done by gross examination and then confirmed with frozen sections of the margins of the cava. In these cases, this translates to about 2 cm or more of normal vena cava above and below the tumor. In all of these patients, the margins were negative.

You also asked what clinically patent meant. These were patients in whom no symptoms of venous insufficiency were seen during the follow-up period; however, we did not have any radiologic confirmation of patency. These patients were three of the eight survivors. Five of the eight grafts were found to be patent, either by duplex scan or by computed tomography scan with contrast. So, at least we have radiologic confirmation of graft patency in five of the eight survivors.

I believe that you are correct in stating that we do not have long-term follow-up in these patients. However, if you look at the oncologic literature on inferior vena cava tumors, the average survival rate is about 16 months. We are now at an average of 21 months survival in patients who have undergone this procedure. We feel confident that the thoroughness of the resection is contributing to survival. We continue to be enthusiastic about this approach and now offer it to patients who have involvement of the vena cava where complete resection requires removal of that structure.

Dr. Robert B. Rutherford (Silverthorn, Colo.). Do you have a control group of patients in whom the tumor was resected and the cava was also resected but not reconstructed for comparison? Also, what are your criteria for deciding that a particular malignant involvement of the cava requires reconstruction? Do you measure pressures or just signs of venous congestion? Is it a decision that you make before or during operation?

Dr. Quinones-Baldrich. These cases are referred to the oncology service. In the past, before 1990, these patients were approached by resection and ligation of the cava. There was concern not only with the relatively poor

survival rate but also with development of venous symptoms, particularly in the first few months after surgery.

These symptoms tend to resolve with time as these patients develop new collaterals. However, the perioperative period was complicated somewhat by lower-extremity edema. It is on the basis of that experience that we started approaching these patients with complete resection and replacement of the vena cava.

We do not have a contemporary or parallel experience with the two approaches. What we have to compare are the results of our prior approach and those presented today. Mean survival has increased by about 5 months. We think this is probably a combination of better resection and avoidance of perioperative edema that was seen after resection and caval ligation.

Dr. Carlos Donayre (Torrance, Calif.). I commend you and your group on a nice presentation. I have a question about the five patients who had radiographic follow-up. Could you comment about whether any of them had the renal veins reattached to the polytetrafluoroethylene graft? If so, did they remain patent? I am not as concerned about patency in the large diameter vena cava as in the smaller renal veins.

Dr. Quinones-Baldrich. One of the patients who had the renal vein attached to the graft has been examined by computed tomography scan. The entire reconstruction was found to be patent. The patient, who had both renal veins attached to the graft, has not been studied radiologically, but his creatinine has remained normal.