Surgical strategy for treating renal cell carcinoma with thrombus extending into the inferior vena cava

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Objective: A surgical strategy for treating malignant renal tumors with thrombus extending into the inferior vena cava (IVC) was assessed.

Methods: We retrospectively reviewed the records for all patients with renal cell carcinoma (RCC; n = 30) or Wilms tumor (n = 1) with tumor thrombus extending into the IVC who underwent surgical intervention at our institution between January 1980 and December 2001. Tumors were classified preoperatively according to the cephalad extension of thrombus, and intraoperative procedures were selected on the basis of degree of extension. Patients with RCC underwent radical nephrectomy and removal of thrombus with (n = 11) or without (n = 19) IVC resection. Partial normothermic cardiopulmonary bypass without cardiac arrest was used in 4 patients. The Pringle maneuver was performed in 8 patients. Infrarenal abdominal aortic cross-clamping was used in 8 patients to maintain systemic blood pressure. IVC cross-clamping and the Pringle maneuver were performed in 5 patients with suprahepatic thrombus extension. Temporary placement of a filter in the IVC or plication of the IVC above the hepatic vein was performed before hepatic mobilization, to decrease the risk for pulmonary embolism.

Results: One patient died intraoperatively of pulmonary embolism. Postoperative complications occurred in 11 patients; all resolved with conservative therapy. The postoperative duration of survival in patients with RCC was 37 ± 44 months (range, 4-180 months); the 5-year survival rate was 42%.

Conclusion: Aortic cross-clamping during IVC occlusion prevented hypotension and maintained hemodynamic stability that has required bypass in other series. This surgical treatment with the less extensive approach could result in long-term survival of patients with RCC in whom tumor thrombus extends into the IVC. We recommend that radical nephrectomy and tumor thrombectomy, with or without caval resection, be performed in these patients, with less invasive additional maneuvers. (J Vasc Surg 2004;39:829-35.)

The most common type of tumor occupying or extending into the inferior vena cava (IVC) is renal cell carcinoma (RCC), and such extension has been observed in 4% to 19% of RCCs.1-8 Tumor thrombectomy in the IVC improved the prognosis in patients with this condition, including those in whom tumor thrombus extends far into the vessel.9 In contrast, if only nephrectomy is performed the prognosis is poor and almost all patients die within a year.10 With the advances in immunotherapy with such agents as interferon,11 control of distant metastases in patients with RCC extending into the IVC can be achieved; thus survival of these patients may increase if aggressive surgery including tumor thrombectomy is combined with immunotherapy. It appears worthwhile to perform thrombectomy even in patients in whom RCC thrombus extends to the level of the right atrium. We reviewed the records for patients in whom this surgical strategy was used, and assessed its effect on survival.

PATIENTS AND METHODS

We retrospectively reviewed the records for 30 patients with RCC and 1 patient with Wilms tumor with tumor thrombus extending into the IVC who were treated surgically at our institution between January 1980 and December 2001. Twenty-two patients were men, and 9 patients were women; their mean age (± SD) age was 63 ± 10 years (range, 23-77 years). Twenty-one patients had stage III disease and 10 had stage IV disease, according to the tumor-node-metastasis classification system. Nine patients were found preoperatively to have distant metastases (Table). Before surgery, tumors were classified into four categories according to the level of cephalad extension of tumor thrombus into the IVC, as described by Naves and Zincke12 (Fig 1). The extension level was determined by using abdominal computed tomography (CT), magnetic resonance imaging (MRI), cavography, and duplex scanning. Tumor thrombus extended from the renal vein into the infrahepatic segment of the IVC, less than 2 cm from the renal vein, in 13 patients (level I); to below the hepatic vein in 9 patients (level II); into the suprahepatic segment of the IVC but not into the atrium in 5 patients (level III); and into the atrium in 4 patients (level IV).

Three patients had leg edema, and RCC extending into the IVC was confirmed in two of these patients. In the third
Findings in 31 patients with renal carcinoma, according to cephalad extension (level) of tumor thrombus into the inferior vena cava

<table>
<thead>
<tr>
<th>Finding</th>
<th>Level I (n = 13)</th>
<th>Level II (n = 9*)</th>
<th>Level III (n = 57)</th>
<th>Level IV (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distant metastasis (no. of cases)</td>
<td>Lung (3), orbit (1)</td>
<td>Lung (2), liver (1)</td>
<td>Right tibia (1)</td>
<td>Left adrenal gland (1)</td>
</tr>
<tr>
<td>Operating time (min; mean ± SD)</td>
<td>284 ± 82</td>
<td>421 ± 66</td>
<td>457 ± 124</td>
<td>609 ± 52</td>
</tr>
<tr>
<td>Blood loss (mL; mean ± SD)</td>
<td>1313 ± 699</td>
<td>4341 ± 1979</td>
<td>3900 ± 2314</td>
<td>7810 ± 4483</td>
</tr>
<tr>
<td>Complications (no. of cases)</td>
<td>ARF (2), ileus (3), cholecystitis (1)</td>
<td>Ileus (2), DVT (2)</td>
<td>None</td>
<td>DIC (1)</td>
</tr>
</tbody>
</table>

ARF, Acute renal failure; DVT, deep-vein thrombosis; DIC, disseminated intravascular coagulopathy.

*For operating time and blood loss, n = 7, because hepatectomy was performed because of liver metastasis in one patient, and hepatocellular carcinoma in another patient, and the data for the two patients were excluded.

†For operating time, blood loss, and complications, n = 4, because one patient died during surgery.

The patient the edema had been subsiding gradually for 6 months and tumor extending into the IVC was not initially found; the patient had been admitted because of another problem. Leg edema was present in only 2 patients admitted because of RCC extending into the IVC, probably because the other patients had adequate collateral draining veins.

During the surgical procedure duplex scanning and transesophageal echocardiography were performed to reconfirm the cephalad extension of tumor thrombus and to evaluate cardiac function. Selection of specific surgical techniques and additional measures was made on the basis of thrombus extension level and the degree of IVC patency. The IVC was occluded in 13 patients, and was patent in 18 patients. Causal tumor thrombectomy and closure of the longitudinal caval incision were performed in 17 patients with a patent IVC, with preservation of the contralateral renal vein, and in 2 patients with an occluded IVC. The other 11 patients with an occluded IVC underwent IVC resection. No IVC reconstructions were performed in this series.

In patients with an occluded IVC, either renal vein ligation or reconstruction was performed, depending on the disease site. If RCC originating from the right kidney extended into the IVC, the left renal vein (LRV) was separated from the IVC because the LRV had several branch veins (adrenal, ovarian, lumbar) draining into the hemiazygos system. On the other hand, if RCC from the left kidney extended into the IVC, the connection between the right renal vein (RRV) and caudal IVC should be preserved, or the RRV should be reconstructed to the caudal IVC because of a paucity of draining veins from the right kidney.

Calligaro et al reported that the LRV could be divided if its stump pressure was about 50 to 60 cm of water (37-44 mm Hg) or lower. Higher backpressure suggests insufficient drainage into the branch veins (adrenal, ovarian, lumbar) and possible risk for renal congestion or renal rupture from high venous pressure. In aortic repair, when the backpressure is greater than 40 mm Hg, reconstruction with an expanded polytetrafluoroethylene graft or direct anastomosis is required. Thus, in our series, stump pressure of 40 mm Hg was assumed to indicate that ligation was feasible, if renal function was satisfactory.

In patients with level III tumor thrombus extension the supradiaphragmatic segment of the IVC was clamped after the pericardium was incised. Measures used to prevent pulmonary embolism were temporary placement (the day before surgery) of an IVC filter and plication of the IVC by inserting 3-0 polypropylene sutures in its suprahepatic or retrohepatic segment. In the 4 patients with level IV tumor thrombus, partial normothermic cardiopulmonary bypass (CPB), without cardiac arrest, and cannulation of the femoral artery and vein and the superior vena cava were performed.

Partial or total abdominal aortic cross-clamping, without administration of heparin, was necessary in 8 patients with a patent IVC, because systemic blood pressure fell below 80 mm Hg during IVC cross-clamping, as a result of decreased venous return. Systemic blood pressure could be maintained at greater than 100 mm Hg by using this method, without CPB. The Pringle maneuver was applied to prevent bleeding from the hepatic vein and hepatic congestion in 4 patients in whom suprahepatic IVC clamping was used and 4 patients who underwent partial CPB.

For the data analysis, the duration of cross-clamping of the abdominal aorta and clamping of the portal vein and hepatic artery, the operating time, the amount of blood lost during surgery, and the postoperative survival duration are expressed as mean ± SD. Survival curves were calculated with the Kaplan-Meier product-limit method. Survival differences between groups were evaluated with the log-rank test. P < .05 was considered to represent statistical significance.

RESULTS

Overall, mean cross-clamping duration was 23 ± 12 minutes (range, 6-45 minutes). Mean duration of clamping of the portal vein and hepatic artery with the Pringle maneuver was 15 ± 1 minutes. The abdominal aorta and IVC were clamped simultaneously if the systemic blood pressure fell below 80 mm Hg. After tumor resection and running suture of the IVC were accomplished, the cross-clamps on the aorta and IVC were released simultaneously.
Operating time and amount of blood lost increased with the level of thrombus extension (Table). One patient died intraoperatively of pulmonary embolism. One patient with RCC on the left side underwent RRV replacement with an expandable polytetrafluoroethylene graft to preserve the venous flow to the IVC through the RRV. Eleven patients had postoperative complications (Table), most commonly, ileus (n = 5). All complications resolved with conservative treatment.

Among the 30 patients with RCC who survived surgery, the postoperative survival duration was $37 \pm 44$ months (range, 4-180 months). The overall 5-year survival rate was 42%. Five-year survival rates for patients with levels I, II, III, and IV thrombus extension were 44%, 53%, 33%, and 25%, respectively (not significant). Five-year survival rates for patients with stages III and IV disease were 49% and 20%, respectively (not significant). The 5-year survival rate for the 18 patients who had renal capsular invasion was 48%, whereas that for the 11 patients without renal capsular invasion was 57% (not significant).

A representative case of level II RCC thrombus extension is shown in Figs 2 to 4. Preoperative abdominal CT scans revealed a large thrombus extending into the IVC (Fig 2, top); cavography showed the thrombus extending to just below the hepatic veins (Fig 2, bottom). During surgery, suprahepatic IVC cross-clamping and the Pringle maneuver were performed at the same time. The systemic blood pressure fell below 80 mm Hg during IVC cross-clamping, because of decreased venous return, but was raised to more than 100 mm Hg with partial or total abdominal aortic cross-clamping, without venovenous bypass or CPB (Fig 3). Tumor thrombectomy was accomplished, and the longitudinal caval incision was closed with running sutures because the IVC was not totally obstructed (Fig 4).

**DISCUSSION**

Berg$^{15}$ was the first to report nephrectomy and cavotomy to treat RCC with tumor thrombus extending into the IVC. Since then, aggressive surgical treatment, including tumor thrombectomy, has improved the prognosis in patients with this serious condition, and it is now used at many institutions.$^{4,6,9}$

In our series, tumor thrombus in the IVC was assessed without difficulty preoperatively with ultrasonography, abdominal CT, MRI, and cavography. The cephalad extension of thrombus into the vessel was confirmed with either cavography or MRI, but MRI is preferred because of its relative noninvasiveness.$^{16}$ The selection of operative procedures was made on the basis of the level of thrombus extension and whether the IVC was patent.

Systemic blood pressure and circulatory status were stably maintained during cross-clamping of the IVC in patients in whom the vessel was completely occluded by thrombus, and the IVC was resected without difficulty. Although Tsuji et al$^{17}$ suggested that total clamping of the IVC below the orifice of the hepatic veins does not induce hypotension or intestinal congestion, systemic blood pressure fell to less than 80 mm Hg at cross-clamping in 8 of the 18 patients with a patent IVC in our series, because of a

Fig 1. Extension of renal tumor thrombus into the inferior vena cava.

Fig 2. Top, Abdominal CT scan in a 58-year-old man with renal cell carcinoma (open arrow) shows a large tumor thrombus extending into the inferior vena cava (black arrow). Bottom, Cavogram in this patient showed a large tumor thrombus extending into the inferior vena cava to just below the hepatic veins (arrow). RA, Right atrium; SHV, short hepatic vein; Rt RV, right renal vein.
profound decrease in venous return. In previous series, hemodynamic stability was restored by creating a venovenous bypass from the common femoral vein to the axillary vein, thereby maintaining venous return.\textsuperscript{18-20} In our series, hemodynamic stability was obtained with partial or total cross-clamping of the infrarenal or supraceliac segment of the abdominal aorta; this maintained systemic blood pressure above 100 mm Hg without any adjunctive procedures, such as venovenous bypass or CPB. This maneuver was based on the method used by Khaneja et al\textsuperscript{21} to control hemodynamic circulation and minimize blood loss, and decreases in blood pressure by cross-clamping the supraceliac segment of the aorta in patients with penetrating injuries of the IVC. Thus, after the infrarenal segment of the abdominal aorta was exposed and encircled with a vessel loop, we cross-clamped (test clamping) the IVC and both renal veins. Blood pressure was then observed for about 5 minutes. If systemic blood pressure decreased to less than 80 mm Hg, the infrarenal segment of the abdominal aorta was partly cross-clamped. If blood pressure could

**Fig 3.** Intraoperative photograph and diagram in the same patient as in Fig 2. The inferior vena cava (IVC) was incised after partial abdominal aortic cross-clamping was performed simultaneously with suprahepatic IVC cross-clamping and the Pringle maneuver. \(A\), site of suprahepatic IVC cross-clamping; \(B\), site of the Pringle maneuver; \(C\), site of right renal vein clamping; \(D\), site of infrarenal IVC cross-clamping; \textasteriskcentered\, site of partial abdominal aortic cross-clamping, which is hidden by the surgeon’s hand.
not be maintained with this procedure, the supraceliac
segment of the aorta was cross-clamped. Supraceliac cross-
clamping should not be continued for more than 30 min-
utes, because longer clamp time may result in renal dys-
function in one kidney.

Interventions that use venovenous bypass to maintain
venous return\textsuperscript{18-20} are complicated and time-consuming. Aortic cross-clamping is simpler, more convenient, and more effective in stabilizing systemic circulation. With this technique Cummings et al\textsuperscript{22} performed nephrectomy, cavotomy, and tumor thrombectomy in patients with RCC with thrombus extending into the intrapericardial segment of the IVC. When vascular isolation of the IVC from the
right atrium to the pelvis was achieved with temporary
circulatory arrest in the lower torso, the circulating blood
volume was divided and blood pressure was maintained.

In patients with tumor thrombus extending into the
suprahepatic segment of the IVC, clamping of the supradi-
aphragmatic segment after only longitudinal diaphragm
and pericardial incision was necessary in this series, whereas
steronotomy and partial CPB was performed by Tsuji et
al.\textsuperscript{17} The CPB procedure increased operating time and
blood loss in patients with level III and level IV thrombus
(Table). Ideally, CPB should be performed only in patients
with level IV thrombus. In our series, partial normothermic
CPB without cardiac arrest was instituted in patients with

Fig 4. Intraoperative photograph and diagram in the same patient as in Figs 2 and 3. Tumor thrombectomy was
performed, and the longitudinal caval incision was closed with running sutures. GB, Gallbladder; Lt RV, left renal vein;
IVC, inferior vena cava.
level IV thrombus, and the femoral artery and vein and the superior vena cava were cannulated. Tsuji et al. commented that partial normothermic CPB without cardiac arrest was used to enable tumor thrombectomy even in patients in whom thrombus did not extend into the right atrium. Others have used CPB with cardiac arrest and deep hypothermia in patients with level IV thrombus. However, these procedures were not required in our patients, because we had no problems with aortic cross-clamping and the Pringle maneuver, which minimizes bleeding from the hepatic vein and prevents hepatic congestion, because the location and numbers of short hepatic veins could not be evaluated and the draining veins could not be confirmed before the operation. Intestinal congestion can be prevented by clamping the superior mesenteric artery.

In our patients tumor thrombus could be peeled off the IVC wall easily, and direct inspection confirmed the absence of residual tumor in the vein. In some patients with levels II, III, or IV disease with a patent IVC, exfoliation of the tumor near the renal vein may be so difficult that both tumor thrombectomy and wedge resection of the IVC should be performed, to completely resect tumor that has apparently invaded the IVC wall around the renal vein orifice. Radical nephrectomy and excision of tumor extending into the IVC, with IVC resection, are advisable in patients in whom the IVC is occluded by tumor thrombus. In our series, only 2 patients in whom the stump of the IVC was left had recurrence of tumor during long-term follow-up. Thus our experience indicates that tumor thrombectomy without IVC resection yields acceptable results in patients with a patent IVC.

In the series of Tsuji et al. venous reconstruction was done in all patients to prevent venous insufficiency. In our series no IVC reconstructions were performed, and no serious postoperative complications occurred. IVC reconstruction was not required, because collateral veins were sufficiently developed to drain the venous return from the lower extremities and pelvic region. In 1 patient in our series a pulmonary embolus developed suddenly while the liver was mobilized. CPB could not be used, and the patient died of a massive pulmonary embolus. Therefore careful skeletonization is important; furthermore, plication should be performed initially in patients with level II or III disease, and in patients with level II disease a filter can be placed into the IVC temporarily. CPB can be used immediately to enable tumor thrombus extending into the intrapericardial portion of the IVC to be mobilized to a more caudal site, and the IVC cross-clamped at that site, because plication can be difficult in some patients with level III disease.

The overall 5-year survival rate in our series was 42%, compared with 34% in the series of Nesbitt et al. Our survival rate was higher, probably because only 1 of our patients had lymph node metastasis. However, immunotherapy with agents such as interferon has improved the prognosis in advanced RCC with tumor thrombus in the IVC. Thus an aggressive surgical approach is warranted.

With both surgical treatment and adjuvant immunotherapy, the 5-year survival rate in patients with liver or bone metastasis, or both, was 17%; in patients with liver or lung metastasis the rate was 43%. Lung metastasis had no adverse effect on survival after surgery. Nephrectomy, tumor thrombectomy, and hepatectomy might be indicated in patients at relatively low-risk with liver metastasis, even though the long-term survival rate in these patients is lower than in patients with lung metastasis, and lymph node metastasis is generally the most important prognostic factor.

In conclusion, selection of the surgical strategy for treatment of RCC with thrombus extending into the IVC should be made on the basis of the level of extension, patency of the IVC, and laterality of the carcinoma. Blood pressure and hemodynamic stability were maintained intraoperatively with partial or total aortic cross-clamping. Partial normothermic CPB without cardiac arrest should be performed in patients with level IV disease. The Pringle maneuver should be applied to minimize blood loss from the hepatic vein and prevent hepatic congestion when CPB is used or the suprahepatic portion of the IVC is clamped. It is desirable to use temporary placement of an IVC filter and plication of the IVC in its suprahepatic or retrohepatic segment to prevent pulmonary embolism. The relatively satisfactory postoperative survival duration and survival rate achieved in our series indicate that nephrectomy and caval tumor thrombectomy, with or without cavotomy, should be used aggressively, with a less extensive approach and less invasive additional maneuvers in patients with RCC with thrombus extending into the IVC.

We thank Kae Yoshizawa for assistance with preparation of the manuscript.

REFERENCES
