A Critical Analysis of Surgery for Kidney Cancer with Vena Cava Invasion

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Abstract

Objective: Patients with kidney cancer with venous system involvement are at high risk of cancer recurrence even after the tumor thrombus is successfully removed. This review analyzes the impact on prognosis of the level of involvement of the inferior vena cava (IVC) in renal cell carcinoma (RCC).

Methods: A literature search was done and relevant papers were reviewed. Relatively recent papers as well as large series or papers from expert centers are included in the reference list.

Results: Venous invasion in RCC is a major challenge for urologists and patients with venous involvement have a worse prognosis. Although successful removal of a tumor thrombus in the renal vein and IVC may result in improved long-term survival in more than half of the affected patients, a higher level of thrombus appears to be a bad prognosticator for cancer recurrence. A complete IVC thrombectomy, even in the metastatic setting, provides a better quality of life and may prolong survival.

Conclusions: Because surgery still remains the most effective therapeutic option in patients with RCC, every attempt should be made to completely remove the IVC thrombus. New targeted agents could be promising as adjuvant therapy in this subset of patients.

1. Introduction

Renal cell carcinoma (RCC) constitutes 3% of all solid neoplasms seen in humans and is an important health problem. There has been a worldwide increase in the incidence of RCC, partly attributed to earlier diagnosis following imaging for non-urologic problems. In parallel with the decrease in the size of incidentally detected kidney tumors, surgery for RCC is also changing from radical
resection to more organ- and function-preserving approaches. Despite earlier diagnosis, up to 10% of patients with newly diagnosed RCC are still diagnosed with renal vein and inferior vena cava (IVC) involvement [1–4].

Because surgery remains the most effective form of treatment for RCC, every attempt is made to render the patient tumor free. This has prompted urologic surgeons to do radical nephrectomy even in the metastatic setting, including metastasectomy of resectable lesions and removal of the venous thrombus in the venous system. The surgical management of RCC with extension into the renal vein, IVC, or sometimes into the heart has always been a technically challenging and demanding operation for urologists. Developments in imaging, anesthesiology, and perioperative care now allow the safe removal of the thrombus, but there is still considerable morbidity and mortality in this type of surgery. A successful IVC thrombectomy provides considerable palliation to the patient and can sometimes lead to higher long-term survival rates. An aggressive surgical resection is proposed when there is IVC involvement because those patients who undergo only nephrectomy all die within 1 yr [5,6].

Patients with venous system involvement are still at high risk of cancer recurrence even after successful IVC thrombus removal. The correlation between the level of thrombus and the rate of survival has been extensively discussed in the literature. This review analyzes the level of involvement of the IVC and its impact on prognosis.

2. Level of thrombus

IVC involvement is more common on the right than on the left side because of a shorter renal vein. Half of the IVC thrombi are infrahepatic and only 10% of them are located in the right atrium. Identifying the extent of IVC involvement is crucial for staging and surgical planning. Although the extent of an IVC thrombus can be identified by abdominal ultrasonography and computed tomography, the sensitivity of magnetic resonance imaging is superior to these techniques and is now the gold standard for assessing the level of IVC thrombus [7]. Inferior vena cavography is not often used. During surgery, transesophageal ultrasonography enables real-time visualization of the thrombus.

A number of classification systems are used for the macroscopic vascular involvement in RCC. The Mayo classification is commonly used (Fig. 1) and consists of four categories based on the extension of the thrombus [8]. Level I is when a thrombus is limited to the renal vein or <2 cm within the IVC. Level II is when the thrombus extends >2 cm within the IVC above the confluence of the renal vein and IVC but is still below the hepatic veins. Thrombus involving the intrahepatic IVC is level III. Level IV is when the thrombus extends above the diaphragm or into the right atrium. The surgical approach strategy is based on the proper assessment of the level of the venous extension.

The most recent TNM classification only distinguishes between T3b tumors that grossly extend into the renal vein(s) or IVC or its wall below the diaphragm and T3c tumors that grossly extend into the IVC or its wall above the diaphragm [9].
3. Surgical treatment

Surgery for IVC thrombus in RCC is a major operation and must be performed by experienced teams in experienced centers. Although most of the cases of minimal IVC extension can be dealt with through commonly used incisions, more extensive IVC thrombus may require different types of incisions and various types of surgical maneuvers such as hepatic mobilization, Pringle's maneuver, and venovenous bypass. Complex supradiaphragmatic and atrial tumor thrombi of RCC are still real challenges for the urologist. Many techniques have been described for the safe removal of these thrombi. Some authors advocate cardiopulmonary bypass with deep hypothermic arrest [10–12], but others advocate alternative techniques that avoid this type of approach, which can be highly morbid [3,5,13–15]. Vena cava resection may be required if the wall of the IVC is invaded by tumor. Recently, there have been an increasing number of reports of laparoscopic treatment of RCC with renal vein thrombosis [16].

Radical nephrectomy with removal of a thrombus from the IVC may be associated with major perioperative morbidity (up to 70%) and mortality (3–16%) [3,5,6,8,11,14,17]. The complication rates increase with the higher extension of the caval thrombus. The most common complication is significant blood loss. Reported transfusion amounts vary between 3 and 70 units [5,11]. The average blood loss is higher in patients with left-sided tumors and with higher levels of IVC thrombus.

4. Prognosis

Although IVC thrombus implies a worse biologic behavior, it does not ultimately affect long-term prognosis [5,12,15,18–20]. Most of the patients with nonmetastatic RCC and renal vein or IVC tumor thrombus can have high progression-free, cancer-specific, and overall survival rates. Three questions have been extensively discussed in the literature concerning the impact of IVC thrombus removal on survival: (1) the impact of thrombus removal in nonmetastatic RCC and the adverse factors for survival; (2) the level of thrombus and its impact on survival; and (3) the impact of thrombus removal in metastatic RCC. These three issues will be discussed in turn.

4.1. The impact of thrombus removal in nonmetastatic RCC and the adverse factors for survival

It is well known that even microscopic vascular invasion in a presumably localized RCC is a poor prognostic factor [21,22]. Thus, poor prognosis is also expected in patients with a macroscopic thrombus in the large vessels. Surgical removal of an IVC thrombus in patients with nonmetastatic RCC should always be attempted to improve survival. Many authors have published series of tumor thrombus removal and the major series are summarized in Table 1. In some of the published reports, patients were diagnosed and treated a few decades ago when imaging, staging, and the quality of perioperative care were not as advanced as today. Even then, the overall survival at 5 yr seems to be >50%. It is evident that in a patient with venous thrombus, surgery with complete removal of the tumor has a major impact on survival. The adverse prognostic features for patients with venous thrombus are perinephric extension of RCC, lymph node metastasis, incomplete tumor or thrombus excision, and invasion of the IVC wall [1,2,5,8,23].

4.2. The impact of the level of tumor thrombus on survival

One of the most controversial topics in surgery for IVC thrombus in RCC has been the level of tumor thrombus and its impact on survival. The TNM staging of T3b and T3c is based on the assumption that a higher level of tumor thrombus is associated with a worse prognosis. Patients with more extensive thrombus propagation tend to have tumors of a higher grade and a more advanced local stage.

Some reports showed lower rates of survival in patients with tumor thrombus in the IVC and in particular in those with higher cephalad extension

<table>
<thead>
<tr>
<th>Author/reference</th>
<th>Year</th>
<th>No.</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skinner [5]</td>
<td>1989</td>
<td>43</td>
<td>5-yr OS 57%</td>
</tr>
<tr>
<td>Galzer [12]</td>
<td>1996</td>
<td>18</td>
<td>5-yr OS 57%</td>
</tr>
<tr>
<td>Moinzadeh [20]</td>
<td>2004</td>
<td>140</td>
<td>5-yr CSS 60%</td>
</tr>
<tr>
<td>Kim [19]</td>
<td>2004</td>
<td>81</td>
<td>10-yr OS</td>
</tr>
<tr>
<td>Lubahn [18]</td>
<td>2006</td>
<td>44</td>
<td>Renal vein 66%</td>
</tr>
<tr>
<td>Giancio [15]</td>
<td>2007</td>
<td>56</td>
<td>IVC 36%</td>
</tr>
<tr>
<td>Wagner [24]</td>
<td>2007</td>
<td>1192</td>
<td>Renal vein: T3c 12%</td>
</tr>
</tbody>
</table>

OS = overall survival; CSS = cancer-specific survival; IVC = inferior vena cava; PFS = progression-free survival.
Skinner et al reviewed data on 56 patients and reported a 5-yr survival rate of 35% for level I, 18% for level II, and 0% for level III patients and concluded that thrombus level was an important prognosticator [5]. Kim et al studied 226 patients with venous thrombus and, after controlling for Fuhrman grade and performance status, they showed that patients with a tumor thrombus in the IVC above the diaphragm had a significantly worse survival rate than those with a renal vein or infradiaphragmatic IVC thrombus [19]. In a recent paper, Ciancio et al reported their experience of 56 patients, in which they found that 10 of 49 patients with level I–III thrombus developed distant metastases during follow-up, whereas 4 of 7 patients with level IV thrombus developed metastases [15]. Other studies did not identify the level of IVC thrombus as a negative prognosticator [12,20]. Glazer and Novick reviewed data on 18 patients with IVC thrombus extending into the right atrium and showed that their long-term survival was not significantly different from that of patients with infrahepatic or retrohepatic IVC thrombi [12]. The overall and cancer-specific 5-yr survival rates were 57% and 60%, respectively. Survival was better in patients without renal capsular extension compared to those with perinephric fat penetration (58.1 vs. 19.7 mo). It is suggested that prognosis is determined by pathologic stage or the IVC wall invasion rather than the level of extension [1]. Moinzadeh and Libertino, in a study of 153 patients, found that a higher level of thrombus was not associated with an increased spread of tumor in the perinephric fat or lymph nodes or with distant metastasis [20]. Five-year cancer-specific survival was similar in all levels of thrombus groups. However, 10-yr overall survival of patients with renal vein invasion only was 66%, whereas it was 29% for thrombus at the level of IVC.

In a recent communication, a retrospective multicenter series of 1192 patients with pT3a and pT3b RCC who underwent nephrectomy was presented [24]. Having taken into account tumor size, perinephric fat invasion, lymph node involvement, distant metastases, and IVC thrombus, the authors concluded that IVC invasion at any level significantly and independently decreased the rate of survival.

4.3. The impact of thrombus removal in metastatic RCC

How should the urologist approach patients with metastatic RCC and venous thrombus? These patients are usually symptomatic and have IVC syndrome, intractable edema, cardiac dysfunction, abdominal pain, or hematuria. Removal of the thrombus, even if it does not cure the patient, may relieve symptoms and provide a better quality of life. However, life expectancy, performance status, and comorbidity should all be taken into account. About a third of those patients with IVC thrombus have metastases. With the advent of new targeted therapies, survival of these patients might be improved with aggressive surgery and medical therapy.

In a series of 30 patients an actuarial 5-yr survival rate of 17% was achieved where 80% of the patients were able to complete adjuvant immunotherapy [25]. Those patients with only lung metastases did much better. Zisman et al, reporting on a series of 207 patients with RCC and venous thrombus, found that whereas 63% of patients with tumor thrombus had metastases at diagnosis, only 25% of a cohort of 607 patients without thrombus had metastases [26]. The overall survival rate of patients with IVC thrombus was similar regardless of metastatic status, and metastatic patients with thrombus who underwent surgery had a significantly better response to immunotherapy than those treated nonoperatively. Thus, the combination of cytoreductive surgery and immunotherapy has an important role in the treatment of patients with renal vein thrombus and a potential role for those with IVC thrombus.

5. Conclusions

Venous invasion in RCC is major surgery for urologists and patients with venous involvement have worse prognostic indicators. Successful removal of the tumor thrombus in the renal vein and IVC may result in improved long-term survival rates for more than half of the affected patients. The higher the level of thrombus the higher the likelihood of cancer recurrence. Removal of the IVC thrombus, even in the metastatic setting, provides a better quality of life and may prolong survival. Because surgery is still the most effective therapeutic option in patients with RCC, every attempt must be made to completely remove the IVC thrombus. New targeted agents may be promising as adjuvant therapy in this subset of patients.

Conflicts of interest

The authors have nothing to disclose.

References


